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A MANUAL

OF

PATHOLOGICAL HISTOLOGY

TO SERVE AS AN INTRODUCTION TO THE

STUDY OF MORBID ANATOMY.

BY

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VOLUME I.

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NOTICE TO THE READER.

The following translation has been executed from the second German edition; those who may compare it with the original will notice that the latter half of § 24 is entirely altered, while an important addition has been made to § 481. These changes were introduced by the author's desire. The second volume is in the hands of the printer.

The translator has to thank Mr. Nettleship for reading through the first twenty sheets as they were passing through the press.

King's College, London,
July, 1872.

AUTHOR'S PREFACE TO THE FIRST EDITION.

In offering a new text-book to the student-youth of Germany, I feel obliged to say a few words about its contents, and the main principles by which I have been guided in its composition.

Pathological Anatomy is one of the youngest branches of Medicine. It was founded by *Morgagni* in his great work: *De sedibus et caussis morborum per anatomen indagatis* (*Venet.* 1761). It was elaborated by its founder and his immediate successors [represented in Germany by *Johann. Fr. Meckel* (*Handbuch der Patholog. Anatomie*, Halle, 1804-5), *Otto*, and others], in entire accordance with the methods of normal descriptive anatomy. During the first thirty years of the present century, it came to comprise a summary of the general alterations to which the various organs of the body are liable in disease; alterations in form, size, number, consistency, continuity, position, relations, colour, and contents. Microscopical investigation, which supplemented the anatomy of *Vesalius* by normal histology, had necessarily to confer a like benefit on pathological anatomy. *Rokitanski* and *Virchow* have rendered undying services to our science as the founders of pathological histology. It soon appeared, however, that pathological histology was destined to stand in a relation to morbid anatomy, very different from that of normal histology in reference to normal anatomy. Pathological histology shows us how the coarser alterations in the size, consistency, colour, &c., of organs, are based upon certain definite changes in their structural elements; it explains the former by means of the latter. As time wore on, it took its place, not merely as an integral constituent, but as the true centre of the entire domain of pathological morphology. The following treatise was undertaken from this point of view; attention has accordingly been directed to the pathological histology in the first place, while the coarser data of morbid anatomy are relegated to the second.

For the benefit of my colleagues, I may add that this book was written in the laboratory rather than in the study. The number of original investigations which it embodies, must serve to atone for the absence of an exhaustive and uniform treatment of individual topics.

AUTHOR'S DEDICATION TO THEODOR BILLROTH

(*Standing in lieu of Preface to the Second Edition*).

My dear Friend,

I very much regret that I was away from home a few weeks ago, when you paid me the visit to which I had long been looking forward. I should have keenly enjoyed discussing with you the great events of this most memorable time, and talking over the little difficulties which beset the author of a hand-book of Pathological Histology, when he desires to keep pace with current discovery.

It is a hard thing to play the part of architect to a building, the materials for which exist only as a heap of stones, more or less roughly hewn; but for which no general plan has been laid down. One has to build in continual peril of having to pull down remorselessly to-day, what seemed but yesterday to be solid and enduring. Compare the section dealing with Morbid Growth in this second edition, with the same section in the first; not one stone has been left upon another. For this we have to thank *Billroth*, *Cohnheim*, *Thiersch*, *Waldeyer*, *Stricker*, *Köster*, and many others. And how long may we expect the present edifice to last? As you know, I am the last man to complain of this. But I should have good reason for complaint, were any one, in looking over this book some years hence, to forget that the views laid down in it were the views of the author in October, 1870. This has been done by some critics of my first edition. On more than one occasion, I have been pained to find myself regarded as "older" than I really was, by a vigorous and energetic youth. I own that

I have myself to thank for some part of this annoyance, inasmuch as I have published but little beyond the present hand-book, during the last few years; I found it more convenient to incorporate the results of my work—so far as they were worthy of such incorporation—into the new edition of the hand-book, than to print them separately. I would therefore ask you to bear this bad habit of your friend in mind, while reading this new edition which belongs to you, and to judge what I have written, with indulgence.

RINDFLEISCH.

Bonn, 1st *November*, 1870.

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INTRODUCTION.

§ 1. Everything that lives is subject to perpetual destruction and renewal of its constituent elements. These changes are inferred from observation; we mark the continual adoption of certain substances into the organism, and the excretion of others in proportionate quantity; these others being demonstrably produced by the metamorphosis of the living substance.

§ 2. The human eye, even when armed with the highest magnifying powers, cannot detect this molecular activity of matter. It becomes apparent to our senses only when it is disturbed, whether in a plus or minus direction. Who can see the nutritive processes taking place in the fibres of striped muscle in the tail of a living tadpole, or note the silent coming and going of matter in a neighbouring connective tissue corpuscle? So long as these structures continue to exhibit, even to the smallest dot and line, a certain definite and familiar aspect, we hold this "morphological permanence" to be a proof that the metamorphoses associated with nutrition are progressing undisturbed. It is only when we discover some qualitative change in the cells or other elementary parts of the organism, that we are made aware of some past or present change in their constitution, and incline with reason to the belief that such change is due to some alteration in the nutritive process.

§ 3. Changes of this kind occur even in the normal course of life. The age of the body, its gradual growth and decay, are to some extent reflected in the condition of the tissues. We must distinguish *in limine* between two leading tendencies, under which all tissue changes may be grouped; these are, development and retrograde metamorphosis. The former teaches us to trace the origin and growth of the entire organism from the repeated multiplication and manifold differentiation of the cell; the latter shows us that the infirmities and the frailty of the body as it grows old are associated with a more or less striking decomposition of its tissue elements.

§ 4. Those alterations in the tissues which occur during disease are of far greater moment to the physician. They are precisely similar to those which occur as a consequence of age. Not without reason has *Virchow* compared the retrogressive processes of disease with a kind of premature old age. The existence of the individual cell, like that of the organism in its entirety, must oscillate between birth and death. We must therefore regard development and decay as the main categories under which all morbid tissue changes naturally fall. But it would be unfair to omit all mention of the fact that the histological phenomena in the domain of pathology are far more various than those attending the normal course of growth and decay.

§ 5. Nearly every disease which is accompanied by anatomical lesions exhibits a complex co-existence and succession of progressive and retrograde processes. To these, taken together, the naked-eye appearances of a diseased lung or liver are due. Our task in the first part of this treatise will be to disentangle the threads of this complicated web, and to examine each of the progressive and retrograde processes singly and from every point of view, so that, in the second part, we may be able to construct the morbid anatomy of particular diseases out of elements which are already familiar.

GENERAL CONSIDERATIONS.

I. THE RETROGRADE METAMORPHOSIS AND DEGENERATION OF TISSUES.*

§ 6. The alterations to be considered in the first division of this work have this feature in common, that the tissues which exhibit them have lost the whole or a part of their significance as living and functionally active constituents of the organism. The degree of this loss is different in each case. Some lead at worst to a certain limited, though perhaps very considerable, impairment of vitality, as, *e.g.* amyloid degeneration and calcification; others again, as, *e.g.* fatty metamorphosis, cause a gradual but complete destruction of the independent life of the affected tissue; under this head, too, we may include necrosis itself—*i.e.* the case in which death precedes, instead of following, the structural change.

We will begin with the last-named process.

1. Necrosis.

§ 7. No sooner does that peculiar inter-dependence and mutual connexion of the component parts of the human organism which results from their genetic unity, and which we call life, come to an end, than external influences assume a dominion over the body similar to that which they exert over inorganic substances; in other words, the only force which still tends to maintain the body in its previous form is the force of cohesion. Owing, however, to the great proportion of water which enters into the composition of the body, this force operates but feebly; hence death is closely followed by disintegration, which, though at first gradual, proceeds at an accelerating rate until dissolution is complete. So long as the body retains to some extent its outward form, we continue to speak of it as "dead."*

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* Nature begins her labours with construction; we adopt the inverse order, taking first the decomposition of structures already formed. This is done for convenience sake. The reader is supposed to be familiar with normal histology, with the materials on which the processes of destruction and dissolution are exerted; and, so far, it would seem to be indifferent whether we choose to start from the progressive or the retrogressive series. Inasmuch, however, as we shall have to describe the histological phenomena exhibited by morbid growths, such as cancer, throughout their entire course, a previous acquaintance with many processes belonging to the retrogressive series, such as fatty degeneration, caseation, &c., is indispensably necessary.

§ 8. In presence of somatic death the art of the physician is powerless. We might spare ourselves the trouble of studying the changes which accompany the death of the tissues, were it not that single portions of the organism are liable to die, an occurrence which we call necrosis, mortification, or gangrene.

§ 9. The death of a part is not always followed by the same series of anatomical changes. The variety of the causes which may lead to necrosis, as well as the situation and individual constitution of the necrosed parts, occasion very marked differences, particularly as regards the proportionate amount of blood and water present, which have led to the recognition of two forms of gangrene, the dry and the moist. In the ensuing sections this distinction will be borne in mind; it will be shown, however, that the distinction is based rather on the clinical characters and coarser features of the process than on its finer anatomy.

Note.—A large majority of the various forms of mortification may be looked upon as due to a complete arrest of nutrition. Among the chief conditions of undisturbed nutrition, a regular and continuous supply of blood takes the foremost place. If, therefore, the quantity of arterial blood which passes through any region of the body (thereby becoming venous) in a unit of time should sink below the normal standard, the nutrition of that region must needs suffer; should the current entirely cease, nutrition must cease with it. The affected part may nevertheless contain an excess of blood; and this may be so great as to give the part a dark purple or livid hue. In such a case, the microscope shows us an extraordinary turgidity of the capillary vessels, associated with minute extravasations scattered throughout the parenchyma; in the smaller veins, which are also gorged with blood, we find blood corpuscles, solitary or in rows, intercalated between the layers of which their walls consist. On inquiring into the cause of such a disturbance of the circulation, we commonly find that the obstacle is situated in the afferent arteries of the part. In a future page, those diseases of the vessels will have to be specially considered, which may give rise either to simple plugging (thrombosis, embolism) or to gradual contraction of the calibre of a vessel, or finally to a condition of its walls which so exhausts the *vis a tergo* of the heart in the larger arterial trunks that it sinks to a mere nothing in the extremities. (*Special Part*, Chap. II.). Enfeeblement of the heart's contractions, consequent upon disease of its muscular substance, or due to general debility, such as follows typhus fever, is also capable of disturbing the circulation in the peripheral parts of the body to such an extent as to cause mortification. Senile gangrene, which affects the toes, feet, and legs as far up as the knees, is commonly caused by the co-operation of both causes, *i.e.* by changes taking place in the muscular walls of the heart, together with disease of the vessels. Compression of the arteries (*e.g.* by tumours from without) must naturally exert a like unfavourable influence upon the circulation within the area of their distribution. Tonic spasm of its muscular coat very rarely contracts the tube of an afferent artery so far as to check the flow of blood through it. Yet gangrene of the extremities, following the consumption of large quantities of ergotized grain, is believed to be due to this cause.

---

* Inorganic nature, into whose domain the constituents of the organism now return, is also called "dead"; but here the term is used metaphorically. In common language, the word "dead" implies that a body, though still exhibiting the organic type of structure, is no longer the seat of the organic functions.

The stoppage of the blood current may also occur in the capillaries themselves. The most interesting example of this is when the capillaries of a part are compressed by exudation or morbid growth in its parenchyma. So in diphtheritic inflammation, an exudation into the substance of a mucous membrane, or of the skin, causes death and sloughing of the part. Moreover, most of the necroses (so-called *κατ᾽ἐξοχην*) of the osseous system come under this head; collections of pus between the periosteum and the bone, due to periostitis, compress the nutrient arteries which pass from the former to the latter, and so deprive the outermost layers of the bone of their supply of pabulum. The formation of pus in the Haversian canals will lead in like manner to squeezing of vessels and death of corresponding portions of bone tissue (caries). It need hardly be added that in these cases no congestion of the necrosed part can possibly occur; on the contrary, we may invariably expect to find a marked degree of anæmia. An obstacle to the escape of blood through the veins rarely causes gangrene. For, to produce gangrene, it seems that the arrest must be complete; and this condition is hardly ever realised. At least we often see thrombosis of all the *greater* veins of the thigh after pregnancy, without its being followed by gangrene of the leg. Indeed, there is only one case which comes under this head, viz. when a part is jammed into a disproportionately narrow and unyielding opening, as, *e.g.* a knuckle of bowel in the neck of a hernial sac. In this case, the yielding walls of the veins undergo compression before the arteries, and so the return of blood may have ceased long before its afflux is at all interfered with. We may accordingly expect to find the mortified part greatly congested.

All the above causes of necrosis agree in making an arrest of the normal flow of blood through a part the proximate antecedent of the arrest of its nutrition and its life. But nutrition may also be disturbed, apart from any interference with the circulation, in the islets of parenchyma which are included in the meshes of the capillary network. Nearly all such troubles, however, are developed gradually; the tissue changes to which they give rise contrast with the necrotic processes in the slowness with which life is extinguished. They will form the subject of succeeding chapters. The only true necroses which come under this head are those involving organs, which, like the cartilages and the cornea, are absolutely non-vascular, when these are wholly separated from their connexion with neighbouring parts by suppuration. The circulation through those vessels which formerly supplied the organs with nutrient matter is not arrested; it is only that transit of pabulum from cell to cell, on which both cartilage and cornea depend for their nutrition, which is brought to a stop.

No allusion has yet been made to those cases of necrosis in which the death of a part is caused by chemical or mechanical agents operating from without, as, *e.g.* crushing, concussion, desiccation, corrosion, and septic poisons. In these cases, we have to do with violent disturbances of molecular arrangement which are incompatible with the continuance of vital activity in any form.

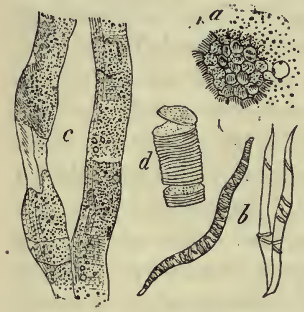
§ 10. A striking peculiarity of living tissues is their power of retaining their form and characters in fluids capable of dissolving albuminous substances and their derivatives. Hence it is a sure sign of death when the tissues are no longer able to withstand the solvent action of such fluids. This feature is common to all gangrenous changes, and it is one which is early recognisable; the dead part loses its normal elasticity, its *turgor vitalis;* it becomes flabby, soft, and doughy. Now, if a too rapid evaporation from the surface of the mortified part is prevented (and this office is performed by the cuticle, when present), we find that the 81 per cent. of water contained in the normal organism, together with the water which is set free on the spot by the very act of decomposition, is amply sufficient to dissolve all the solids of the body with the exception of the bones. We already know, moreover, that in most cases of gangrene the vessels of the mortified part are unusually gorged with blood.

Now, the blood contains more water than any other tissue of the body. Hence the mortified part will contain more than its due proportion of water, at the expense of the healthy tissues; it is therefore all the more able to undergo solution in its own fluids.

The remaining naked-eye appearances are also due to this excess of blood. For, soon after death, the colouring matter of the blood deserts the corpuscles, and stains, first the serum, and next all those tissues which are naturally either colourless or nearly so. It saturates the walls of the vessels and the lax connective tissue round them, so that the course of the veins may be traced by the purple streaks and patches to which the livid marbling of the skin in gangrene of external parts is due. Finally, every part becomes equally saturated with blood, the fat of the *panniculus adiposus* not excepted. In external parts, the reddish serum makes its way to the surface of the cutis. The previous disintegration of the *rete Malpighii* favours a loosening of the impermeable cuticle, so that the accumulation of serum may occasionally lead to the production of what are known as gangrenous blebs; more commonly, however, it simply strips off the cuticle in large shreds. In the latter event, unless evaporation be otherwise checked, a rapid desiccation of the most superficial parts—of those which are open to the air—takes place. Impregnated as they are with blood pigment, they present, when dried, a very dark, nearly black colour (Gangræna sicca; mummification.) Putrefactive changes are temporarily arrested wherever desiccation has occurred. Desiccation, therefore, is at once a means of killing living parts, as we see whenever a scab is formed, and of protecting parts already dead from further decay. The following statements, therefore, concerning gangrenous changes in tissue, are all conditional on the presence of water in sufficient quantity for the solution of the parts; they apply, therefore, to gangrene of internal parts, and to that of external parts, in so far as these are not exposed to desiccation.

§ 11. The blood is the first of the tissues to undergo decomposition. A few words are enough to describe the morphological phenomena of the process. I have already said that the blood pigment forsakes the corpuscles and is gradually imbibed by all the tissues of the mortified part. We shall have to trace its farther destiny hereafter. The colourless protoplasm swells up moderately and ceases to be visible. In a short time not a single unaltered blood corpuscle can be found.* In certain exceptional cases we may find blood corpuscles of an intense brown tint aggregated together in masses of variable size, even in advanced stages of mortification. The edges of such masses are almost always scalloped (fig. 1, *a*); the outermost layer of corpuscles is seen breaking up into minute coloured granules; and this mode of decomposition may be regarded as the ultimate fate of all.

Fig. 1.



Gangrenous disintegration of the tissues. *a.* Masses of aggregated blood corpuscles; *b.* Fibres of unstriped muscle; *c.* Fibres of striped muscle; *d.* Their break-up into Bowman's discs, $\frac{1}{300}$.

§ 12. Changes taking place in NUCLEATED CELLS constitute a second group of the phenomena incident to necrosis. We may start with the general proposition that the death of a lump of nucleated protoplasm is followed by its speedy dissolution. Its disintegration is ushered in, and in some measure facilitated, by a phenomenon which we have long recognised in the fibres of striped muscle as "rigor mortis," and which consists essentially in a coagulation of those semi-fluid, viscid, albuminous matters in which all the formed constituents of the cell—(in the present case the nucleus and protoplasmic granules)—are embedded.

---

* It has been experimentally shown by *Alexander Schmidt* that in a layer of blood barely a line thick, which is in contact with air, but not allowed to evaporate, the blood corpuscles soon disappear; in dogs' blood this takes from fifteen to eighteen hours, in horses' blood about three days, in ox blood, however, not less than eight or ten days. The blood first assumes a lake tint; we then (in the blood of the dog) see the blood corpuscles first losing colour, then changing form, and appearing more numerous by isolation. The decolorised discs are then wholly dissolved. The decolorisation of the corpuscles, the passage of the colouring matter into the serum, and the solution of the colourless stroma, are all results of oxidation. (*A. Schmidt,* "Minor Researches in Physiological Chemistry." *Virchow's Archiv,* xxix.)

By this coagulation the protoplasm is rendered incapable of movement; it stiffens in an attitude which corresponds to the "quiescent state" of the cell; the granules, too, which may previously have exhibited some sort of molecular movement, become stationary; the whole structure puts on a dull and dusty look,* finally breaking up into granules of large relative size, which then shrink and disappear. The nucleus, which was at first rendered more distinct, also falls a prey to this disintegration.

§ 13. The course of events is naturally modified in accordance with the previous physiological development of the cells. Our description is unconditionally applicable to the cells of the connective tissue, of the rete Malpighii, and of those deeper layers of other epithelial membranes which correspond in position to the rete; also to the secreting cells of glands, and to lymph corpuscles. But the limitary membrane with which the older epithelial cells are furnished offers a strenuous resistance to the solvent process. Hence these cells retain their form long after their nucleus and their protoplasm (here=cell-contents) have been broken up into granules; so that epithelium cells, destitute of nuclei, are constantly to be met with in mortified parts. In this respect the cells of the epidermis take a foremost place; the duration of their resistance to the necrotic process being proportionate to the degree of their cornification.†

§ 14. The FIBRES OF UNSTRIPED MUSCLE, though not endowed with a limitary membrane, retain their peculiar aspect for a comparatively long time; their nuclei are often only to be traced by an elongated mass of dots, while their marginal outlines are still as distinct as ever. The phenomena of rigor mortis have been but little studied in the contractile substance of unstriped muscle. Our only data on this subject are those given by *Heidenhain.** He describes certain phenomena of coagulation in the fibres of unstriped muscle, occurring from sixteen to eighteen hours after death. The cells first assume a granular or sandy aspect, due to the presence of a countless number of minute, dark, punctiform bodies throughout their contents. These molecules, which are too small to be measured, unite to form shaded figures of an irregular outline, which in their turn coalesce to form coarser, highly refracting, elongated, straight or curved particles, embedded in a residual substance of greater transparency. These particles are sometimes irregularly distributed throughout the cell, sometimes disposed with tolerable regularity in transverse lines equidistant from one another, giving the cell a coarsely striated appearance (fig. 1, *b*). I can confirm these statements from observations of my own. This mode of decomposition may constantly be observed in cases of so-called softening of the stomach; a tumefaction and solution of the gastric walls, formerly regarded as due to disease, but which is now known to be of post-mortem origin (*Elsässer*—fig. 1, *b*). The altered muscular fibres are farther destined to be converted into a viscid, mucoid substance, in which, however, the dot-like bodies described above long continue to be visible.

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* *Kühne* failed to observe this change in the cells of the areolar connective tissue, but he saw it in the corneal corpuscles of the frog. (*W. Kühne*, "Researches on Protoplasm and Contractility." Leipzig, Engelmann, pp. 121-130.)

† We must bear in mind, however, that cornification is itself a gradual transition from life to death. I may add, by the way, that during cornification a shrinking and final disappearance of the nucleus may also be observed.

§ 15. The phenomena of necrotisation in the FIBRES OF STRIPED MUSCLE are far more complex than those which have just been described. This is a fit occasion for discussing the phenomena of rigor mortis in greater detail. From twelve to fourteen hours after death, all bodies, with the exception of those killed by charcoal fumes, sulphuretted hydrogen, or lightning, or which have succumbed to putrid fevers and the exhaustion of lingering maladies, pass into a peculiar state of rigidity which lasts for about twenty-four hours, and which resolves itself, on closer investigation, into a well-marked shortening, thickening, and stiffening of the voluntary muscles. We find a like state of the muscles in limbs whose blood supply has been very suddenly cut off; and we can induce it experimentally, not only by cutting off the supply of blood, but also by the application of heat and cold, by overexertion, mechanical violence, and chemical agents, and most rapidly of all, by means of distilled water.

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* *Heidenhain,* "Coagulation of the Contents of the Contractile Fibre Cells after Death." (Researches in the Physiological Institute at Breslau, i. 199.)

Numerous researches, the latest and most exhaustive of which we owe to *W. Kühne* (*l. c.*), render it certain that this rigidity of the muscular fibres is immediately due to the precipitation of a solid albuminous constituent from the muscular fluid. This muscle clot (myosin of *Kühne*) forms a white and not very transparent mass, and so causes marked opalescence of those muscles which are in a state of rigor mortis, complicated, moreover, by a shade of brown.

Now, although rigor mortis is the first step towards death, it is a step which is not irretrievable. It is quite possible to throw a frog's leg into a state of rigor mortis by tying the afferent vessels, and then to watch it resume its normal condition on removal of the ligature. Should the case be one of permanent death of the muscular fibre, the rigidity is followed by decomposition. The naked-eye phenomena of this farther change are, first, the fading of the bright red colour of the muscular tissue, which is replaced by a dirty red, or yellowish grey tint, unless it happen to be saturated with dissolved hæmatin; secondly, the cohesion of the muscle is impaired to such an extent that it finally becomes converted either into a greasy, jelly-like mass, in which no trace of its former fibrous structure can be detected, or into an easily torn, dirty grey, tindery substance, in which some indications of longitudinal striation are still to be found. The microscopic appearances are even more constant. The transverse striæ and nuclei are masked by a cloud of minute dark specks; oil globules, and granules of reddish pigment appear partly within, partly outside, of the contractile substance; the latter is torn across at intervals; the fragments melt away from their edges to their centre; the sarcolemma holds out longest, and when it finally succumbs to the common fate, it contains only a few small, shapeless fragments of its former contents, which mingle with the rest of the *débris* (fig. 1, *c*).*

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* *Falk* states (*Centralblatt*, 1866, p. 434) that the transverse striæ approach nearer to each other before they are swallowed up in the cloud of granules, and that the complete solution of the fibres is not infrequently preceded by a longitudinal splitting of the contractile substance.

It is only when the above mentioned jelly-like condition of the decaying fibres is especially well marked that we may expect to find the manner of their dissolution somewhat modified. It was in a case of fairly circumscribed gangrene of half the foot, due to frost-bite, that I first noticed that condition, and with it a break-up of the fibres into Bowman's discs; since then I have had an opportunity of confirming my original observation (fig. 1, *d*).

§ 16. Nothing is at present known about the necrosis of NERVE-CELLS, and very little about that of the peripheric NERVE-FIBRES. We know that the thicker nerve-trunks maintain themselves in the interior of gangrenous parts for a relatively long time, while, on the other hand, their finer branches undergo very rapid decomposition. It is probable, from the analogy of rigor mortis, that a coagulation of the medullary substance precedes any farther changes. Accordingly the fluid matter between the axis cylinder and the neurilemma, which is normally quite homogeneous, runs together to form globules of various sizes, which are separated by a clear fluid. The dark and wavy outlines of these drops impart a highly irregular aspect to the entire fibre (fig. 8, *a*), which has not inaptly been compared to the spiral curls of smoke from a pipe. We are still ignorant of the chemistry of the phenomenon; we do not know whether the drops of myelin (*Virchow*) are to be viewed as a deposit from the medullary substance, or merely as a change in its mode of grouping,* the observation itself being as old as *Leeuwenhoek*. The farther progress of putrefaction is indicated by a general tumefaction of the nerve-trunk, in consequence of which the individual fibres grow very dim and the neurilemma indistinct, while the axis cylinder entirely disappears. Complete liquefaction occurs at some points sooner than at others; this gives the fibres a varicose appearance, like that presented by the fibres of voluntary muscle shortly before their complete disintegration.

§ 17. THE ADIPOSE TISSUE plays a far more important part in the course of mortification. The liquid oil readily escapes from the cells which normally contain it; the liberated oil globules coalesce to form larger drops, giving the *sanies gangrænosa* (§ 22) the peculiar aspect of an emulsion, and permeating all the mortified tissues so thoroughly, that it becomes very difficult to get a specimen all whose chinks and crevices are not occupied by a countless multitude of oil globules.

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* *G. Walter* suggests (in *Virchow's Archiv*, xx. 426) that a coagulation of the albuminoid substances present in the medullary sheath may cause the separation of the oily matters soluble in ether, the latter uniting to form globules of appreciable size.

If we bring the adipose tissue itself under the microscope, we hardly see a single fat-cell which still retains its normal amount of oil; it must, however, be added that it is equally hard to find one which has parted with the whole of its contents. The contained oil globules are mostly reduced to half their usual size; they are often broken up into smaller globules. This residual oil is peculiarly prone to imbibe hæmatin, so that not only the cell membranes and the lax connective tissue between the clusters of fat-cells, but the entire *panniculus adiposus* becomes stained of a red, or reddish yellow colour. Crystals may form in the interior of the cells; but they are far more often to be found in the oil which has been set free; hence they are a constant ingredient of the gangrenous sanies (see § 23).

§ 18. The first change exhibited by the fibres of the LOOSE CONNECTIVE TISSUE is a simple swelling. This does not add to their transparency, like the swelling caused by acetic acid; on the contrary they become more opaque, and refract light more highly. This change is usually associated with the imbibition of blood pigment, alluded to above, the depth of colour produced varying inversely as the amount of water present. For it need hardly be explained that the degree of swelling is exactly proportionate to the quantity of water in the tissue. The evaporation and re-absorption of the fluid from the parenchyma are at once announced by a corresponding desiccation of the fibrillæ of the connective tissue. The coal-black substance into which the cutis is converted by dry gangrene exhibits, in fine sections, a ruby-red colour by transmitted light.

Should the fibres continue to swell, they become granular, their outlines wax indistinct, and they finally melt away into a turbid slime.

§ 19. The formed constituents of the connective tissue offer a far more vigorous resistance than its basis substance. I refer less to the glassy, homogeneous membranes (capillaries, tunicæ propriæ, basement membranes), concerning whose fate during mortification we possess no reliable data, than to the FIBRES AND NETWORKS OF ELASTIC TISSUE. Their notorious indifference to chemical reagents of all sorts is equally shown towards the feebler agencies at work during mortification. The physician confidently anticipates that pulmonary gangrene will reveal itself without the possibility of error by the appearance (among other symptoms) of the elastic elements of the lung tissue in the patient's sputa. Should the elastic fibres, however, become involved in the destructive process, they begin by losing their normal elasticity; they become limp; often, too, they swell, and may ultimately be converted into a jelly-like substance.

Those firmer and more compact fibrillæ of connective tissue of which the TENDONS are composed, and which also occur in fibrous membranes (dura mater, tendinous, muscular and arterial sheaths, periosteum), behave like the fibres of yellow elastic tissue. The first indication which these structures (I refer more particularly to the tendons) present of being involved in moist gangrene, consists in an unravelling of the parallel bundles of fibres from one another; this must be ascribed chiefly to softening and disorganisation of the connective tissue intercalated between them, in which the vessels run. At a later stage, however, the so-called secondary and tertiary fibrillæ are separated from one another, and the tendon is converted into a shaggy mass of fibres, which bears the same relation to its normal structure that carded hemp bears to a well-twisted rope. Even in this stage, however, the tendon, as a whole, is not easily torn; it is only at a much later period that the fibres begin to break up into single granular and beaded strips; these, in their turn, melt away into molecules of minute size, and so become invisible.

§ 20. CARTILAGE is one of the most indestructible tissues of the body. The chemical composition of the inter-cellular substance is very stable, and this, perhaps, is the main reason why large pieces of cartilage, *e.g.* detached articular surfaces, resist necrotic disintegration for long periods of time. When this ultimately prevails, it mostly takes the form of a gradual peripheric liquefaction, during which the cartilage becomes transparent and assumes a reddish tinge. This colour cannot certainly be supposed to be due in all cases to imbibition of the red colouring matter of the blood; this hypothesis is discredited by the fact that the tint in question is constantly exhibited by the cartilages of the larynx and trachea, when these are isolated by suppurative perichondritis. The microscope displays a granular opacity of the inter-cellular substance, which melts away at its edges into a gelatinous mass. The cartilage cavities are generally full of oil globules, due to fatty degeneration of the contained cells; these oil globules are set free when the tissue is finally dissolved.

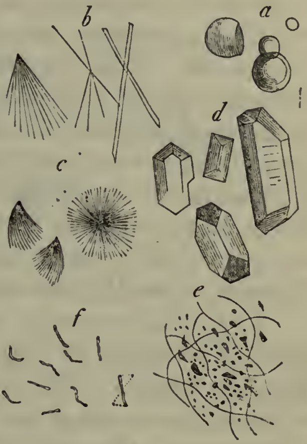
§ 21. BONE TISSUE remains unaltered during necrosis. The surgeon who, amid the most striking variety of inflammatory and ulcerative changes in a bone, recognises a portion of it as the dead part, the sequestrum, by its smooth surface and unaltered form, has every reason to rely on the truth of the above statement. Meanwhile, it is right that we should clearly understand how far we may apply this doctrine of the "unaltered state" of bone tissue in its literal sense. Of course we must always be prepared to meet with those changes in the fragment of necrosed bone which are common to all the bones of the skeleton during somatic putrefaction. Cells, vessels, and medullary tissue all disappear. It would seem, farther, that a great part of the organic matrix, the bone cartilage (ossein), is destroyed by putrefaction, the amount destroyed being proportionate to the length of time during which it has been exposed to the disorganising influence. But for this it would not be possible to account for the notable fact that the specific gravity of sequestra is always far below that of normal bone. Cases occur, moreover, in which the sequestrum, owing to a gradual corrosion of its surface, loses not only its original polish, but also a part of its bulk. Indeed, it is hard to see why complete solution of the necrosed bone tissue should not take place under suitable conditions. The presence of even a minute proportion of some acid in the fluids of the part would suffice to bring this about; and the earthy salts once dissolved, the residual ossein would not offer any greater resistance to putrefaction than articular cartilage and other allied structures. In the meantime, we must rest content with the facts as they stand. As regards the mode in which the disintegration of bone takes place (which, be it said in passing, is nearly the same in dead as in living bones), this will be dealt with elsewhere. (See softening of bone, rarefactive ostitis, caries, &c.)

§ 22. Having thus reviewed the various modes in which the individual tissues break up, let us glance at the fluid which is from henceforth their common rendezvous, and which may be regarded as the organism in solution, though of course not in the sense in which *Moleschott* has employed the phrase to designate the blood. The composition of the SANIES GANGRÆNOSA naturally varies with its place of origin; mortification of lung tissue will obviously yield a fluid differing in some respects from that which results from gangrene of external parts. We may say generally, that it has a foul odour and a loathsome greyish yellow colour; the latter assuming a rosy hue on the addition of nitric acid, as was first noticed by *Virchow*. Even its reaction is not always alkaline. This, together with all the other differences exhibited by various specimens of the fluid, is due to differences in its chemical composition, to which we will therefore first devote our attention.

§ 23. We have already seen that the putrefactive process may physically be defined as a solution of the constituent elements of the body in water; chemically, it may be viewed as a new combination of the elements among themselves, and with the oxygen of the atmosphere. Every chemical substance which enters into the composition of an organ is in a state of perpetual tension; *i.e.* its atoms tend spontaneously to group themselves otherwise than they *are* grouped. Life consists in their inability to carry this tendency into effect; their doing so is a sure sign of death. A series of decompositions and recompositions ensue, which differ for all the different constituents of the body, such as albumen, fat, &c., but all of which ultimately issue in the formation of carbonic acid, ammonia, and water. As this series of phenomena is attended by a large consumption of oxygen, it might be regarded broadly as a process of slow combustion (eremacausis). The transitional compounds, of which there is undoubtedly a great variety, are still to a great extent unknown. Some are volatile, and when produced in abundance give rise to the emphysematous variety of gangrene (*Rauschbrand*); they cause the stench which offends our nostrils (sulphuretted hydrogen, ammonia, hydrosulphate of ammonia, valerianic and butyric acids); others are non-volatile and soluble in water; others again are deposited in a solid form, so that after the complete disappearance of the structural elements of the tissues, a new set of microscopic objects make their appearance; of these the following present most points of interest:

α Leucin, produced in gangrene of the lungs, liver, spleen, and pancreas; it separates in the form of a whitish, opalescent substance, in homogeneous drops or spherules, or in concentrically laminated corpuscles, or finally in knobs of slender, needle-shaped crystals (fig. 2, *a*).*

Fig. 2.



Products of gangrenous decomposition. *a*. Leucin; *b*. Tyrosin; *c*. Fat-crystals; *d*. Ammoniaco-magnesian phosphate; *e*. Gangrene-corpuscles (black pigment); *f*. Vibriones, $\frac{1}{300}$.

β Tyrosin, commonly found with leucin, in the form of white needles with a silky lustre; these are either solitary, or when of considerable length and thickness, united to form sheaves and stars of great beauty (fig. 2, *b*).

γ Margarin. A crystalline mixture of two solid fats, stearin and palmitin. It is peculiarly abundant in mortified tissues. It occurs in needles, either isolated or in clusters radiating from a common centre (fig. 2, *c*).

δ Triple Phosphate—ammoniaco-magnesian phosphate—occurs only in alkaline or neutral sanies. The forms which it most frequently assumes are modifications of the rhombic vertical prism, which closely resemble coffin lids (fig. 2, *d*).

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* *Virchow* says, with reference to the intimate connexion between these divers forms (*Archiv* viii. 337): "On allowing leucin to crystallise from solution, we always see, to begin with, very minute roundish granules appearing in even the smallest drops of a viscid material, differing from oil globules by their feebler lustre and paler outline. Two or more of these frequently unite to form large drusy (*i.e.* studded with minute crystals) figures, or shoot into radiating clusters. If crystallisation proceeds very slowly, they remain more independent; their individual growth making them assume, more and more distinctly, the form of faintly yellow spherules, which often exhibit in addition a concentric lamination. They often show no sign of their being made up of a number of minute needles; on the other hand, masses of closely-packed

ε Pigment Granules, which, with the exception of iron sulphide, are all derived from the colouring matter of the blood, are found in the shreds which float in the sanies oozing from vascular parts, and in the tissues of such parts themselves. They exhibit a high degree of polymorphism. The most frequent variety is a rust-coloured pigment, occurring in the form of granules, either single or aggregated, varying from a yellow to a dark reddish-brown tint; this is closely related to hæmatin in chemical composition, and is also met with in non-gangrenous, so-called pigmentary metamorphoses of tissue, associated with hæmatoidin. It is only what are known as gangrene corpuscles that are regarded as peculiar to necrosis; these are minute black particles of very irregular shape, only to be detected under high magnifying powers, and which set most reagents at defiance. It is by no means certain that these gangrene corpuscles are exclusively associated with putrefactive changes; on the contrary, there are good grounds for believing them to be identical with Melanin, of which more will be said hereafter (fig. 2, *e*).

§ 24. The occurrence of living organisms in gangrenous parts is deserving of especial notice. I have shown already that the process which we call putrefaction (Fäulniss), and which plays so great a part in necrosis, is exclusively due to the presence and the vital activity of these humble organisms. Manifold have been the disputes as to the animal or vegetable nature of the minute, staff-shaped corpuscles which we see in a state of continual rotatory, gyratory, or to-and-fro movement (fig. 2, *f*). Even now that we know all about their development, this question cannot be considered settled. They originate as follows: their germs—dotlike particles of extreme minuteness exhibiting lively movements—settle at the junction of the putrefying body with the air; these germs become elongated, and undergo repeated constrictions, forming long, jointed threads, which are subsequently broken up into their component joints; these constitute the staff-shaped Bacteria. They form a

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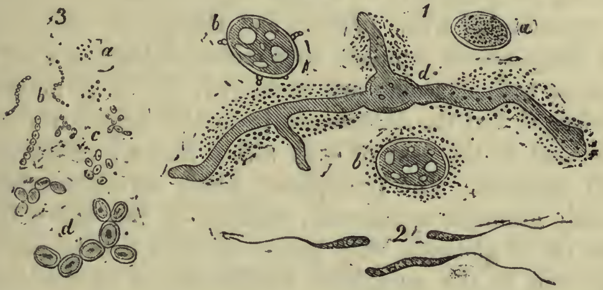
needles may be produced, whose surface is studded with distinct projecting points." The larger spherules may also cohere. In doing so they flatten each other; so that we not unfrequently come across spherules flattened on one side, which have become accidentally detached during mounting (fig. 2, *a*).

greasy scum on the surface of the putrefying substance, penetrating into it to a depth of several lines. They consume a great deal of oxygen, which they obtain for the most part from the proximate principles of the organic matter, thereby causing their decomposition. We cannot allow them to be regarded merely as products of putrefaction; neither can their presence upon the putrefying body be considered as purely accidental. A body may undoubtedly undergo decomposition in other ways as well, but it can only "putrefy" with the aid of Bacteria.

Fig. 3.



(1) Spores and mycelium of Bothrytis acinorum cultivation in an infusion of flesh. *a.* A recent spore; *b.* The same after four hours; *d.* After forty-eight hours, both covered with vibriones, $\frac{1}{500}$. (2) Vibriones set free in an infusion of flesh from the mycelia of mucor, $\frac{1}{800}$. (3) Growth of yeast from germs of vibriones. *a.* Germs; *b, c, d.* The same as vesicles which progressively increase in size, ultimately forming the well-known cell-colonies of yeast. (After *Lüders.*)

2. Conditions of Involution.

a. *Fatty Degeneration.*

§ 25. I have chosen to term the tissue changes, to which the following paragraphs will be devoted, "CONDITIONS OF INVOLUTION," implying thereby that they agree in the association of a gradual metamorphosis and final annihilation of normal structure, with a corresponding diminution and final abolition of the normal function of the affected parts.

§ 26. This definition applies in the first instance to a metamorphosis of CELLS, which is characterised by the appearance of oil globules in their interior, and which has therefore been called FATTY DEGENERATION.

There was a time when men disputed whether the dark-bordered droplets of oil, white by reflected light and soluble in ether, originated in the cell contents, or in the nucleus, or even in the nucleolus. At the present day, though no one would think of denying the possibility of a fatty degeneration of the nucleus, or of its nucleolus when present, and though we must assume that in every case of complete fatty metamorphosis of a cell both its nucleus and nucleolus are destroyed, yet it is universally acknowledged that the disturbance invariably begins in the protoplasm, and in the case of cells with a limitary membrane, in the cell contents. The protoplasm, which normally exhibits a very finely granular appearance, contains at first but a limited number of oil globules, little groups of from two to ten being usually seen in the immediate neighbourhood of the nucleus. These globules never unite to form larger drops, a phenomenon which is constantly exhibited by such particles of oily matter as have penetrated into the cell from without (see below, fatty infiltration); they remain isolated from one another by thin layers of protoplasm. The more numerous they become the narrower grows the outermost zóne of the cell, which is still free from them; at length this vanishes, and the oil globules reach the border of the cell. At the same time the nucleus, which had hitherto been recognisable as a bright spot amid the dark mass of oil globules, and which could be rendered evident by coloration with carmine, ceases to be visible (compare with this and the following sections, fig. 4).

§ 27. During the occurrence of these changes the cell has increased often to three or four times its former size; it has, moreover, become perfectly spherical, and this, whatever may have been its previous shape, whether cylindrical, squamous, or fusiform. It is now known as a "granule-cell,"* and this term must therefore be taken to denote a spherical aggregation of oil globules, held together by an albuminoid basis.

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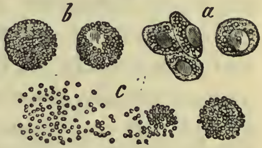
* The term "granule-cell" is decidedly preferable to the older expression "inflammatory corpuscle." *Gluge*, who found these corpuscles in the lung at the outset of pneumonic infiltration, regarded them as

The presence of a large number of these granule-cells gives the fluid in which they are suspended, or the tissue in whose interstices they lie, a yellowish-white or butter-yellow tint. Thus the colostrum, *i.e.* the milk which is secreted during the first few days after confinement, is not white, but yellowish and glutinous: it separates on standing into a clear serous portion, and a creamy fluid which rises to the surface. The latter is almost entirely made up of granule-cells, which owe their origin to a fatty degeneration of the glandular epithelia, and are called colostrum corpuscles. In like manner (to confine ourselves to physiological examples) the corpora lutea of the ovary owe their name to a fatty degeneration of the cells of the membrana granulosa, which takes place in all Graafian follicles which have expelled their contents and are undergoing retrograde metamorphosis.

FIG. 4.



Fatty metamorphosis. Epithelium of pericardium from a case of effusion into its sac. *a.* Cells which still exhibit their normal form and arrangement: first appearance of oil globules; *b.* Granule cells, one of which still exhibits a central nucleus; *c.* Granule cells breaking up into oily *débris.*

§ 28. The last stage of fatty degeneration may be appropriately called "emulsification." The granule cells break up, owing to the solution of their albuminoid cement in the surrounding fluid, which always has an alkaline reaction. A lively oscillation of the oil globules (molecular movement of *Brown*) announces their imminent disintegration; the outermost globules next become detached from the circumference of the cell, and are uniformly distributed through the surrounding fluid, while the residual aggregate undergoes progressive diminution, until at length it disappears, without leaving a trace behind. (This succession of phenomena may be admirably seen in the cells of cancer juice.) The fluid emulsion in which the oil globules are

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characteristic of inflammation. They were afterwards shown to be nothing more than the epithelial cells of the lungs in a state of fatty degeneration, freed from their attachments by the œdema which precedes the inflammation, and so destroyed.

now suspended, the oily detritus, has its physiological prototype in the secretion of the mammary gland; the more uniform distribution of the refracting particles giving it a whiter, or even absolutely white, colour, just as in emulsions which have been artificially prepared.

§ 29. If we inject milk into the abdominal cavity of a rabbit it disappears very quickly; it is still more rapidly absorbed from the subcutaneous areolar tissue. Milk, therefore, and consequently all fatty *dêbris*, are capable of being absorbed, and are usually absorbed, unless absorption is prevented by some exceptional conditions. One of these deserves especial notice, viz. when the products of fatty degeneration are enclosed in a cavity whose walls are in a state of inflammatory irritation, and consequently inclined rather for productive than for absorbent activity. Those products have, under such circumstances, to undergo a farther series of changes. The fatty matters are partly saponified, partly deposited in those solid forms with which we became acquainted during our study of necrosis. Finally, an abundant deposit of cholesterin crystals takes place; these give the dirty-white mass (whose consistency, according to the amount of fluid present, may be either friable or pulpy) a peculiar lustre (atheromatous pulp—atherombrei—grützbrei).

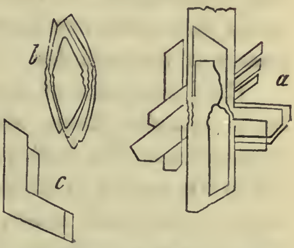
Cholesterin, which we now meet with for the first, though not for the last, time, is still, notwithstanding numerous investigations, a very enigmatical substance.

Its presence in the brain and spinal cord, under perfectly normal conditions, in enormous quantity (40 parts in 1,000) does not allow us to dismiss it summarily as an excrementitious substance. Its constant presence in the biliary secretion is readily accounted for by the fact that the bile is one of the few fluids which is capable of holding it in solution. Chemistry informs us that, besides the bile, it is only solutions of soap and fatty oils which can dissolve it, and these only to a limited extent.

This high degree of insolubility in animal fluids is one of the most striking properties of cholesterin; it is the cause of our so often meeting with it in a solid state.

The regular crystalline form which it assumes is that of a rhombic plate, whose angles are uniformly $=79° 30'$ and $100° 30'$. These plates tend to form aggregates with their longer sides parallel, but without overlapping each other at every point. The various and interesting forms assumed by this substance have been exhaustively studied by *Virchow;* we must, however, refer our readers to the accompanying woodcut and to the original paper (*Virchow's Archiv*, xii. 101). Micro-chemical reactions are very useful in enabling us to distinguish cholesterin with certainty from other substances which have the same crystalline form. These reactions are very characteristic. A drop of concentrated sulphuric acid, when allowed to flow gradually over the specimen, effects a progressive liquefaction of the cholesterin plates at their edges, and makes them assume a greasy appearance. After a little while the plate becomes flexible and quasi-membranous; it is occasionally folded on itself; sometimes it shrinks together; gradually, however, we see the mass melting at its periphery, while a dark reddish-brown globule is formed (*Virchow*, *Wurzburger Verhandlungen*, 1850, Bd. i. s. 314).

FIG. 5.



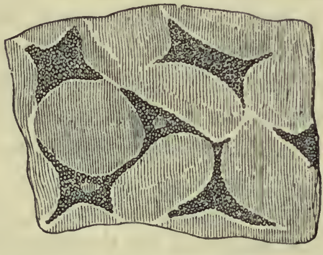
Crystals of cholesterin, after *Virchow.*

The simultaneous action of sulphuric acid and iodine produces a fine blue colour during the first stages of the decomposition of the cholesterin. As regards the presence of cholesterin in the atheromatous pulp more particularly, the hypothesis that it is first taken up by the oily and saponaceous constituents of the emulsion, and then deposited when these are decomposed, undoubtedly accords best with what we know of its properties; but this is a point which requires further investigation for its settlement.

§ 30. We have hitherto traced the course of fatty metamorphosis mainly as it occurs in individual cells. We have yet to show how the phenomena of the process are modified in accordance with the primary modifications in the form of the corpuscular protoplasm. These modifications are, of course, purely morphological. Thus, for example, we cannot expect the aggregation of fat-granules to be perfectly spherical when the original cells are stellate, with long processes; far removed, therefore, from the primitive spheroidal type. We may take the degenerated connective tissue corpuscles of the innermost tunic of the vessels as an example of the polygonal figures in which the granules may congregate. In like manner the fibres of unstriped muscle retain their primitive spindle shape after they are converted into masses of fat-granules.

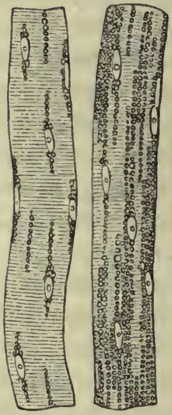
The protoplasm of the fibres of striped muscle has a peculiarly complex form, which is retained even after their fatty degeneration. The doubly refracting sarcous elements (*Bowman*), which we regard as embedded in the protoplasm, constitute, in their longitudinal order, the "varicose fibrillæ" of authors; and these are so disposed in the primitive fasciculus that their nodal points and their constrictions respectively lie in the same planes. Now, if we assume that the space which is necessarily left vacant in this arrangement of the sarcous elements is occupied by the viscid protoplasm, we must needs infer that the latter forms a system of varicose threads with chamfered edges, which are in contact with one another where they are thickest, in those planes, therefore, in which the varicose fibrillæ are thinnest. Larger accumulations of protoplasm exist only in the immediate neighbourhood of the nuclei, which displace the fibrillæ at those points where they are embedded, producing thereby fusiform spaces, which have to be filled in with protoplasm. It is in these little conoidal appendages of the nuclei that the first

Fig. 6.



Connective-tissue corpuscles of the tunica intima in a state of fatty degeneration, $\frac{1}{300}$.

Fig. 7.



Fatty degeneration of fibres of striped muscle, $\frac{1}{300}$.

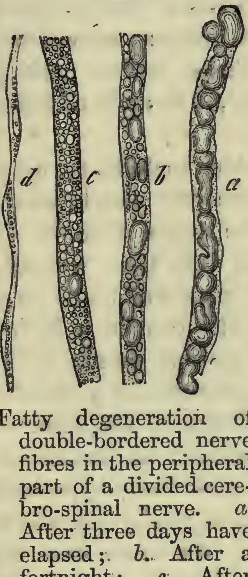
oil globules make their appearance. We see them arranged in very fine and delicate beaded rows parallel with the long axis of the primitive fasciculus, and coinciding precisely with the varicose threads of the interfibrillar protoplasm. The transverse striæ which, after all, are merely due to the uniform arrangement of the more highly refracting particles, must naturally grow indistinct in proportion as the yet more highly refracting fat-granules predominate, and so impair the effect of the groups of disdiaclasts on light (*Brücke's* disdiaclast groups—sarcous elements). In very advanced cases of the disease we see nothing but the oily *débris*, contained, like some fluid, in the tube of sarcolemma (fig. 7).

§ 31. The physico-chemical processes which underlie the fatty degeneration of cells have not, as yet, been very clearly ascertained. We may, however, repudiate the notion that the oil globules penetrate into the interior of the cells from without; against this view we have the fact that muscular tissue in a moderate state of fatty degeneration does not contain a higher percentage amount of fatty matter than normal muscle. The only remaining alternative is that the oil globules are generated in the cell itself. But are they to be viewed as the result of some disturbance in the nutrition of the cell, or as products of the decomposition of its substance? The most likely hypothesis is that we have to do with phenomena diametrically opposite to those which accompany cell development. We know from the composition of the yelk that the material of which the cells are built up consists of albuminous compounds, with a rich admixture of fatty matter. Further, we learn by chemical analysis that healthy muscle contains a considerable proportion of invisible fatty matter; so that we are justified in assuming the existence of an amalgam-like compound of fat and albumen in cells. Fatty degeneration would thus be a "decomposition" of this amalgam, the liberated oil appearing in the protoplasm in the form of globules of appreciable size. The simultaneous enlargement of the cell is explained when we reflect that the same quantities of fat and albumen require more space when separate than in their previous state of intimate combination.

§ 32. The minute changes which take place in the distal end of a divided nerve would powerfully corroborate the views enunciated above, were it clearly proved that the coagulation of the nerve-medulla described in § 16 ought to be regarded as the first step in the dissociation of an amalgam of albuminoid and fatty matter. For, by the common consent of all those authors who have occupied themselves with this subject, the subsequent changes are only a continuation, or, in other words, a carrying out of that still enigmatical phenomenon.

The large dark-bordered drops of myelin break up in the course of from two to four weeks into globules of progressively smaller size, which can no longer be distinguished from oil globules, either by their microscopical or their micro-chemical characters. Side by side with them minute protein molecules of a paler tint make their appearance; a fatty and granular *detritus* results, which remains enclosed for a time in the tubes of neurilemma, and is ultimately absorbed. The axis cylinder remains intact for about six weeks in the disintegrating medullary sheath. If at any time during this period the connexion of the peripheral portion with the central stump is re-established, the sheath fills again with medullary matter, and the axis cylinder resumes its interrupted functions; in the contrary event it becomes granular and splits up, even before the absorption of the oily *débris* is quite accomplished. The empty neurilemma now collapses into longitudinal folds, exhibiting here and there an elongated mass of fat granules, in the interior of which a nucleus may be demonstrated with carmine.

Fig. 8.



Fatty degeneration of double-bordered nerve fibres in the peripheral part of a divided cerebro-spinal nerve. *a.* After three days have elapsed; *b.* After a fortnight; *c.* After three weeks; *d.* After two months, $\frac{1}{300}$.

§ 33. The fatty granular metamorphosis, or *caseation* of cells, may conveniently be regarded as a variety of fatty degeneration. The latter term is that chosen by *Virchow;* it is based upon a close resemblance between the yellowish white, dense, homogeneous, rotten, or greasy mass, which is the final product of this metamorphosis and certain sorts of cheese.

It used formerly to be thought that the substance in question could only result from antecedent tuberculous disease; it used to be viewed as a direct excretion of the *materies morbi* from the blood, and was hence denominated "crude" or "raw" tubercle. The term "tuberculisation" was nearly synonymous with what we now call caseation. *Reinhard* was the first to overthrow the belief in the specific character of this deposit; he erred, however, in declaring it to consist invariably of inspissated pus. It was reserved for *Virchow* to place the matter in its right light, by describing "cheesy necrosis" as a tolerably widespread mode of degeneration of tissues rich in cells.

§ 34. The reader will recollect that in describing fatty metamorphosis, I stated that the presence of a certain quantity of water was essential for the actual disintegration of the cells, in order to dissolve the albuminoid material which held the oil globules of the granule cells together. Should this fluid be wanting, as happens when large masses of newly formed cells are traversed by few or no pervious vessels, the process of fatty metamorphosis is somewhat modified; the two modes standing in much the same relation to one another as that in which dry gangrene stands towards the moist variety. The cells dry up, they shrink into comparatively small, shapeless, mostly angular bodies, in which, besides the oil globules, a considerable number of granules—the so-called protein molecules—may be distinguished. The less the amount of water present, the more does the whole wither into a dense, yellowish-white mass, in which the remnants of cells can be demonstrated, even after the lapse of years. True, we are unable to restore the withered cells to their old shape by the addition of water; this usually breaks up the molecular aggregates, forming a sort of emulsion. Similar changes occur if the cheesy matter should subsequently absorb moisture and soften in the organism itself.

This constitutes, as we shall see hereafter, a most destructive episode in the history of tuberculosis; the softening occurring by preference in such portions of the cheesy deposit as come to the surface on the walls of the internal cavities of the body, whether in the respiratory or digestive tract, and are accordingly exposed to other sources of moisture besides the nutrient juices in which they are bathed. In parts which do not communicate with free surfaces, as in the lymphatic and mesenteric glands, in the bones, the brain, and spinal cord, softening of the cheesy deposits is far less common. On the contrary, an increase in density, a true petrifaction, often ensues, especially in cheesy lymphatic glands, owing to a deposition of calcareous salts in their interior.

§ 35. In conclusion, let us glance at the causation and the distribution of fatty metamorphosis. In the foregoing paragraphs we have often had occasion to touch on these points; now, therefore, we may content ourselves with a general review.

First, then, we may regard fatty transformation as being a regular mode of the retrograde metamorphosis of many tissues which are subject to rapid nutritive change. Among these, the epithelial structures naturally take a leading place. If we moisten the surface of any serous membrane and scrape it with a scalpel, the fluid we obtain will seldom fail to exhibit a certain number of epithelial cells which have undergone fatty degeneration, side by side with others which are perfectly normal.

The epithelium of the mammary and sebaceous glands is peculiarly liable to undergo fatty metamorphosis in the ordinary course of events; so also that of the lungs, and the renal epithelium of dogs and cats. Whether the white blood corpuscles, on completion of their span of life, finally succumb to fatty degeneration, is a question which must be left open; it is an undoubted fact that a certain number of granule cells are constantly met with in the blood of amphibia; but these may of course have originated in the epithelial lining of the vessels.

The fatty metamorphosis which forms an element in senile decay is intimately connected with the above varieties. The enfeeblement of nutrition due to old age is especially manifested in parts where arrangements for the transport of nutrient matter are most complicated by nature, and in a certain sense most difficult.

I allude, of course, to those great tracts of non-vascular tissue which occur in cartilaginous organs, and the transparent media of the eye. Hence it is that we so often find the cells of the laryngeal and tracheal cartilages in old people in a state of fatty degeneration, the capsules being occupied by one or more oil globules. To this group also belongs the *arcus senilis*, a fatty degeneration of the corneal corpuscles adjoining the sclero-corneal junction, and the *gerontoxon lentis*, an opacity situated at the junction of the posterior surface of the nucleus of the crystalline lens with its cortical portion; an opacity which remains stationary for a long time, but which ultimately results in the formation of grey cataract.

But the non-vascular tissues do not stand alone in this respect; nearly all the tissues of the body, nay, even the vessels themselves, are liable to fatty degeneration in consequence of old age and analogous conditions of debility due to exhausting diseases. The muscular substance of the heart is especially subject to this morbid change.

As this, however, is not the place for an exhaustive treatment of the subject, but only for a general review of it, I hasten on to the last and most important—namely, the exclusively pathological category of fatty metamorphoses. This includes all cases of disproportion between the means of nutrition and the parenchyma to be nourished. Such a disproportion may be caused either by a diminution of the *nutriens*, or by an increase of the *nutriendum*. If a minute vessel in the brain is plugged, the circulation in the area which it supplies is not wholly suspended, owing to the manifold anastomoses with neighbouring vessels; nevertheless, a very considerable retardation of the current takes place, which may even give rise to temporary stasis, and to hæmorrhage; and this suffices to disturb nutrition, and so to cause fatty metamorphosis (yellow softening).

The disturbance in the circulation, associated with inflammation, exercises an influence not less hurtful upon the nutrition of parts. Here, too, the amount of pabulum is inadequate. Moreover, inflammation combines this with another cause of disturbed nutrition, *i.e.* an increase in the amount of parenchyma requiring nourishment. The mere œdema of the latter acts in this way; but the chief factor in the production of retrograde metamorphosis is in this case, as in that of many tumours (*e.g.* cancerous and tuberculous formations) the massive proliferation of corpuscular elements.

B. *Cloudy Swelling.*

§ 36. We give this name to an acute swelling and granular cloudiness of the protoplasmic mass, which appears to depend on the precipitation of certain albuminous matters held in solution by the juices of the protoplasm. The change varies in degree from a slight, finely granular cloudiness, without any increase in volume or alteration in shape of the cells, to a granular opacity which entirely conceals the nuclear structures, and is associated moreover with a very marked enlargement and filling out of the corpuscular elements. The granular matter is dissolved by acetic acid; this renders it impossible to mistake the change in question, at least in its earlier stages, for fatty metamorphosis. At a later period such a mistake is all the more likely to occur, inasmuch as the cloudy swelling, unless checked at once, the cells being restored to their normal condition by solution of the contained granules, passes directly into fatty metamorphosis and consequent disintegration.

§ 37. The pathological significance of cloudy swelling was interpreted by *Virchow*, who was the first to describe the process (in the year 1850) as a nutritive irritation of the cells, *i. e.* a stimulation of the cells to absorb an excessive amount of pabulum. It is still admitted to be a consequence of the irritation of cells; and it is notorious that the direct action of various mineral, vegetable, and animal poisons is capable of producing cloudy swelling of the glandular epithelia. (*See* Parenchymatous Inflammation of Liver and Kidneys.) But the question whether the process is active or passive in its nature tends more and more to be answered in the latter sense; so that for my own part I am inclined to suppose a kind of corrosive action, in consequence of which the albuminous matters, held in solution by the protoplasm, undergo coagulation, and become visible as minute granules; the phenomenon being in this respect analogous to rigor mortis.

C. *Mucous Softening.*

§ 38. This constitutes another of the "conditions of involution" to which the tissues are liable. The group of changes embraced under this head involve a gradual liquefaction of tissue, rendered possible by the passage of the insoluble albuminous matters which constitute the cellular and intercellular substance into soluble modifications. Among the chemical compounds which result from this transformation, *mucus* takes a prominent place, inasmuch as its capacity of swelling by imbibition makes it occupy a relatively large amount of space, and so renders it conspicuous even to the naked eye.

§ 39. The chemistry of mucous softening needs only a passing mention at our hands. Taken broadly, it is founded on those protean changes which the nitrogenous, histogenetic substances undergo in the interior of our organism, and which manifest themselves to us as so many variations on a given fundamental theme, a theme for which our search has hitherto been fruitless.

The soluble peptones and alkaline albuminates contained in the gastro-intestinal tube are primarily converted into the seralbumen of the blood. This accompanies the nutrient fluid into the parenchyma of all the organs, and, on becoming solid, serves as material for the construction of the tissues. We find it, least modified, in the protoplasm of the cells; while the collagen and chondrigen of the intercellular substances differ markedly from the albuminates in their reactions, and may hence be termed albuminoids. The transformation into mucin which collagen and chondrigen undergo during mucous softening, renews their affinities with albumen; mucin, however, contains no sulphur; in other respects it exhibits an unmistakable analogy to the albuminates, both in its elementary constitution and in its behaviour towards alkalies. All natural solutions of mucin have an alkaline reaction; indeed mucin is soluble only when combined with a free alkali. For if a solution of mucin is treated with acetic acid it grows viscid in proportion to the amount of alkali neutralised, until at length it separates in thick flakes. It is this last property which more especially connects mucin with the albuminates. For these, too, occur only in the alkaline fluids of the organism, and we know that some part of them at least is held in solution by free alkali. This part behaves almost like an organic salt, in which the place of the acid is taken by the albuminous body (acid-albumin of *Panum*); hence it is termed alkaline, or sodic albuminate.

True sodic albuminate thus constitutes the first and last member of the series of metamorphoses associated with mucous softening. This gives a high degree of probability to that affinity between mucin and the albuminates on which I have already laid stress.

Sodic albuminate differs from ordinary albumen by its greater solubility in water, and also by the greater readiness with which it parts with its water. If crystals of common salt are placed in a fluid containing an alkaline albuminate, the latter separates as a white, finely granular scum in proportion as the salt is dissolved. To this property must also be ascribed the readiness with which the so-called "casein pellicles" form on the surface of solutions of albumen in alkalies, when these are evaporated; casein, according to the most recent researches, being identical with alkaline albuminate. The production of this substance is, therefore, the last step in a cyclic series of metamorphoses which begin with the conversion of the casein of milk (lactation) into the albumen of the blood (the material of which the cells, and the collagen and chondrigen of the intercellular substances, is built up); these in their turn passing into mucin, and so back again to casein. Physiological chemistry can point to more than one series of this kind. The albuminates may be converted into mucin directly, without passing through the intermediate stage of gelatin-yielding matter, as is proved by the development of mucin in the epithelium cells of mucous membranes. The mucin stage, too, may be omitted; we saw this in the case of fatty degeneration, when the protoplasm of the cells was transformed directly into a substance soluble in alkaline fluids, which served to hold the oil globules together. On the other hand the place of mucin in the chemistry of softening may be taken by other albuminoid bodies; as, for instance, by pyin, which is developed, together with mucin, during the purulent liquefaction of connective tissues. The enigmatical albuminoid basis of colloid degeneration also belongs to this series; it will have to be considered separately.

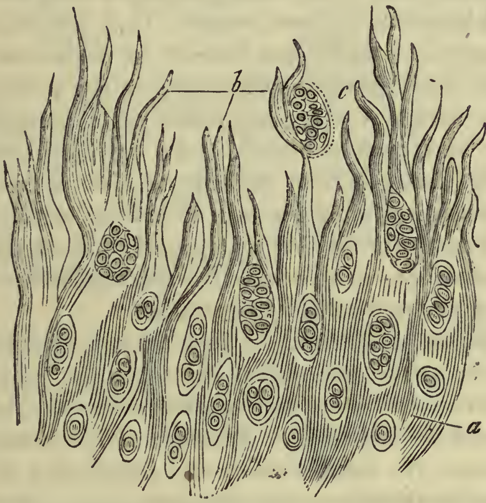
§ 40. In proceeding to discuss the morphology of mucous softening, we are met by two leading problems. What are the phenomena attending the disintegration of existing tissues? What new forms are produced by their metamorphosis?

To the first of these questions we find a definite, though perhaps inadequate answer in the history of mucus-formation on the surface of mucous membranes, and in that of the softening of cartilage and bone.

It is an established fact that the mucus which covers the surface of our mucous membranes is produced on the spot by epithelial cells. By adding a sufficiency of water to the detached epithelia, the formation of large spherules of clear mucus in the interior of the cells may actually be followed under the microscope; they push aside the other cell contents, together with the nucleus, making them look like mere appendages; they finally escape, leaving the body of the cell in a very mutilated condition. This simple experiment is enough to demonstrate the presence of mucus in the interior of the epithelial cells. We are tempted to see analogies between the development of mucus in the protoplasm of these cells, and the cornification of epidermic cells; and the chemical similarity between mucin and keratin yields especial weight to this view.

Then indeed the development of mucus might be conceived as a mucous transformation, and we might even assume with *Frerichs*, *Donders*, and *O. Weber*, that a given quantity of secreted mucus represents a proportionate shedding of epithelial cells, that the epithelial cells are actually shed during the development of mucus.

FIG. 9.



Softening of cartilage. Vertical section through an articular cartilage in senile arthritis (malum senile articulorum), $\frac{1}{300}$.

I cannot give an unconditional assent to this doctrine. I incline rather to the belief that the mucus is, as a rule, simply extruded from the cells, and that a total transformation of cells into mucus occurs only in exceptional cases (as *e.g.* in mucous catarrh).

§ 41. The visible phenomena attending mucous softening of the matrix of cartilage are physiologically exemplified in the symphysal and inter-vertebral cartilages. *Luschka* has justly characterised the changes caused by age in the last mentioned structures as tending to produce an imperfect articular cavity (Gelenkhöhle).

The cavity is produced by a gradual softening of the cartilaginous investment (überzug) of the opposed surfaces of adjoining vertebral centra. The anatomical appearances presented by this, as by every other form of softening in cartilage, are highly characteristic. The homogeneous matrix exhibits dark striæ at right angles to the free surface, which prove at a later period to be the initial stage in the splitting up of the tissue into fibres. The real fibrillation then ensues, beginning at the free surface; the individual fibres separate from one another and float loosely in the articular fluid; their free extremities soon become acuminated and terminate in blunt points. It is here that the intercellular substance undergoes solution in the course of mucous softening. The accompanying process in the cartilage cells exhibits the characters of a progressive, not a retrograde change, inasmuch as a proliferation of cells by fission takes place; the result being, that instead of single cartilage-cells, groups consisting of from two to twenty cells are formed. These cell-nests, surrounded by a capsule and a residue of intercellular substance, mingle with the fluid products of softening, where they undergo colloid degeneration.*

The process of softening in bone tissue is complicated by the necessity for a previous solution and removal of the earthy salts with which its matrix is impregnated, before the liquefaction of the matrix itself can begin. We often find, however, that these two processes, viz. decalcification and liquefaction of matrix, are so nearly simultaneous, that the bone tissue at the limit of absorption is bounded by a perfectly sharp line, curiously indented,† and that no peculiarity in the process of disintegration can be observed. In one case only, that of the atrophic disease of bone long known as Osteomalacia, do we find the solution of the earthy salts separated by a comparatively long interval of time from the liquefaction of the ossein (bone-cartilage).

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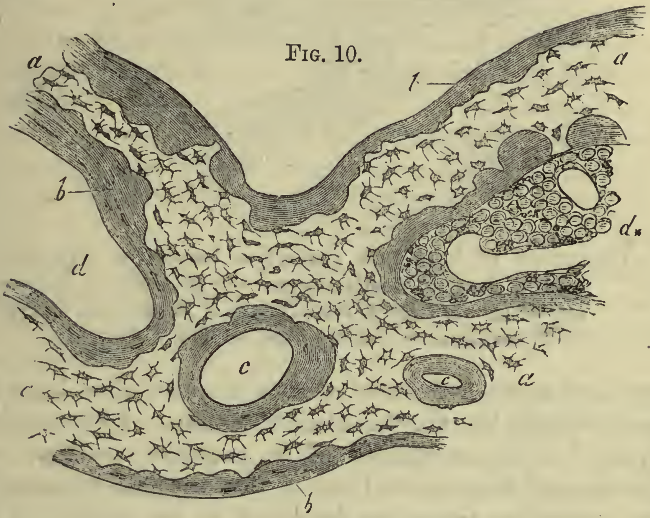
* I cannot assent to *Kölliker's* ingenious theory, according to which the numerous white corpuscles which may be seen, even without the aid of a microscope, in the central jelly of the inter-vertebral discs, are descended from the original cells of the notochord. From the analogy of morbid softening of cartilage, I regard them as being nests of cartilage cells liberated by softening of the matrix, and subsequently affected by colloid degeneration.

† What are known as *Howship's* lacunæ (fig. 10) are due to the unequal rate at which the decalcification of the osseous tissue proceeds. The direction of the stellate processes of the bone corpuscles, with reference to the surface from which resolution is proceeding, seems to exert some sort of guiding influence in the matter. (Cf. Diseases of Bone.)

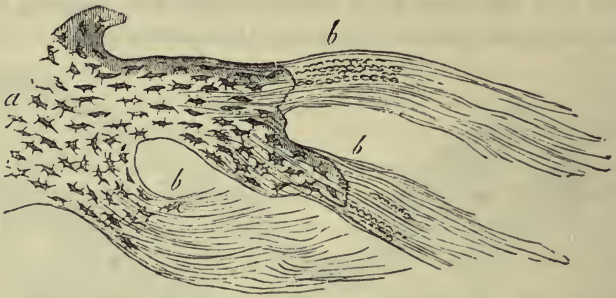
FIG. 10.



Mollities ossium: splinter from the spongy substance of a rib affected with the disease. *a.* Normal bone tissue; *b.* Decalcified bone tissue; *c.* Haversian canals; *d.* Medullary spaces; *d**. A medullary space filled with red marrow: the lumina of the capillary vessels are gaping, $\frac{1}{300}$.

In mollities ossium, therefore, we are able to demonstrate in each trabecula of spongy tissue, or of compact tissue which has become spongy, a broad zone of decalcified ossein surrounding the hitherto unaltered bone tissue on all sides. The ossein, which is now the immediate subject of the liquefactive process, exhibits a striation parallel to the lamellæ; and this striation must be regarded as analogous to the parallel dark lines which we described in the matrix of softening cartilage. That the striation is a sign of incipient fibrillation in this as in the former case, we gather from the evidence of cases in which the bone tissue wastes and disappears under the pressure of tumours growing in its immediate neighbourhood. If we examine the bone in the vicinity of such a tumour, by removing the periosteum, and then breaking off chips of the compact tissue with pincers, and putting them under the micro-

FIG. 11.



Conversion of bone into connective tissue: a chip taken from a sternum wasting under the pressure of an aortic aneurism. *a*. Normal bone tissue; *b*. Bone tissue deprived of its earthy salts and breaking up into fibrillæ, $\frac{1}{300}$.

scope, we may satisfy ourselves that the decalcified bone tissue passes directly into fibrillar connective tissue. I have convinced myself, by the examination of an exquisite specimen in the Pathological Museum at Giessen, that capsular membranes of true connective tissue are developed in the interior of bones around centres of softening in osteomalacia, by a metamorphosis exactly similar to this. Within these capsules the medullary tissue, transformed into a reddish pulp, passes by insensible gradations into a thin, colourless serum (cystoid degeneration of bone).

§ 42. The facts in the preceding section, drawn from the morbid anatomy of atrophic changes in bone and cartilage, comprise what little we know of the visible phenomena of softening in intercellular substances generally. They consist for the most part of simple tumefaction with obliteration of the old forms. We are far more thoroughly acquainted with the new forms which result from the presence of mucus in the various organs and tissues.

Mucus is capable of great increase in bulk by imbibition; the smallest quantities of it suffice to saturate a relatively large amount of water. Such saturated solutions vary in consistency from a viscid jelly to a glutinous synovia, which can be drawn out in threads.

It is still doubtful whether we are justified in calling them "solutions;" some authors wholly deny the solubility of mucus in the physical sense of the term. So much is certain, that mucus is a member of the colloid group of *Graham*,* and that among colloids it takes a leading place. Mucus possesses hardly any diffusive power; this property has important bearings on its development in the organs generally, and it is of especial moment with regard to softening. We may assert, from an *à priori* consideration of its colloid nature, that mucus, as such, can never pass from the blood-vessels into the tissues, or from the tissues into the blood-vessels. The homogeneous wall of the capillaries would not allow it to pass in either direction.

Now, as we never find any trace of this substance in the blood, we are justified in assuming that mucus is invariably a local product, and that it will remain where it is first formed until it is either removed mechanically, or transformed into some material capable of being absorbed.

This incapacity for reabsorption is of little moment when the development of mucus takes place on a free surface. To this category belong not only the physiological secretions of mucous membranes, in which the epithelial cells act as mucus-secreting organs, but also some of those processes which come under the head of softening, *e.g.* the mucous metamorphosis of fibrinous false membranes, and other fibrinous deposits occurring in the course of inflammatory disorders of the respiratory tract. But the incapacity for reabsorption displayed by mucus gives rise to marked and characteristic morphological effects when mucus is developed in the interior of the body, whether in a closed cavity or as a substitute for tissues which have undergone destruction, as in the case of the softening which we are now considering. In such cases it qualifies mucus for the fulfilment of a task which is performed in a higher degree only by "colloid" matter. It enables it, namely, while itself amorphous, to form an integral constituent even of permanent textures, serving to fill up all interstices with its semi-fluid substance.

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* "Annalen der Chemie u. Pharmacie," Bd. 121, s. 1. *Graham* draws attention to the difference in diffusive capacity between colloids and crystalloids. The crystalloids diffuse rapidly and with ease; the colloids little or not at all. To the latter category belong gum, starch, dextrin, mucus, albumen, and gelatin (*Leimstoffe*).

In this connexion the development of mucous tissue takes a leading place. Following *Virchow*, we apply the name to a connective tissue whose matrix has undergone mucous softening, and whose corpuscular elements, owing to this softening or "swelling by imbibition," are pushed asunder to some extent, without necessarily undergoing any alteration in their form. Mucous tissue is much more widely distributed in the embryo at an early stage of its development than in the adult organism. The whole of the subcutaneous areolar tissue is primarily a subcutaneous mucous tissue. At birth, apart from the Whartonian jelly of the umbilical cord, we find only one portion of residual mucous tissue, but that an important one, in the vitreous body of the eye; this retains a singular stability of composition to the end of life.

In the pathological field the production of mucous tissue is far more manifold. We have tumours (*Myxomata*) which are wholly made up of mucous tissue; and others, such as enchondromata, lipomata, and sarcomata, which undergo a secondary conversion into mucous tissue. Mucous tissue is a constant element in syphilitic gummata, and it is occasionally found in fungoid granulations and other growths of an inflammatory origin. We defer a detailed consideration of these various modes of its production till we begin the study of inflammation and tumours.

Of the remaining morphological effects due to the incapacity of mucus for reabsorption, we need allude in this place only to its *cystic* and *cystoid* deposits; the former determined by occlusion of the excretory ducts of glands, the latter by circumscribed softenings of the connective substance. The latter form, with which alone we are now concerned, differs from mucous tissue in its mode of origin. The cells take a less neutral, and more of an active or passive, part in the process, in consequence of which they may either assume greater mobility, appearing as floating elements in the "fluid products of softening," or they may undergo complete destruction.

§ 43. Our ignorance of the conditions which determine the occurrence of mucous softening is nearly absolute. Were it not for the fact that it converts things possessing a sharply defined anatomical form into substances which are amorphous, homogeneous, and capable of absorbing fluid, we might feel doubts about including mucous softening among the varieties of retrograde metamorphosis. The characteristic fact remains, that mucous softening of the connective tissues may take place on the one hand, without any important alteration in the form and arrangement of the cells (mucous tissue), and on the other hand, in connexion with the most various progressive and retrograde changes in them.

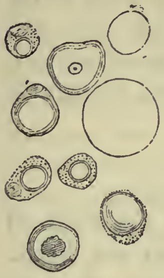
D. *Colloid Degeneration.*

§ 44. We come now to the last member of the series of "Conditions of Involution" to which the tissues are liable. COLLOID DEGENERATION is closely related to mucous softening. Their respective appearances, both naked-eye and microscopic, are in some specimens so much alike, that a long period elapsed before men learned to distinguish between a connective tissue whose matrix had undergone mucous softening and one whose cells had undergone colloid degeneration. The superficial resemblance between the two, gave rise to the greatest confusion in the nomenclature of tumours; the terms colloid, collonema, sarcoma gelatinosum, hyalinum, carcinoma colloides, being indiscriminately applied to one or other variety. What is the basis of this similarity? We find in either case a transparent, swollen, tremulous jelly, traversed by a network of fibres. Now, the mere discovery that in the one case the network was made up of stellate anastomosing cells, while in the other it consisted of the residue of a fibrillated matrix, sufficed to compel the separation of colloid from mucous tissue, a separation which was justified by further researches. In the first place, colloid degeneration is characterised by the presence of a chemical compound, differing from mucin by its neutral attitude towards those reagents which act upon mucus, *e.g.* acetic acid, as also by its elementary composition, which places it among those albuminates which contain sulphur.

Not less important for the independence of colloid degeneration is the fact that, in its first stage at least, it is always a metamorphosis of cells.

This brings us at once to the essential feature of its anatomy. The only form in which colloid matter presents itself to the microscopist is that of a colourless, transparent globule, with an oily lustre, the so-called "colloid sphere." How

Fig. 12.



Cells undergoing colloid degeneration. From a colloid cancer.

do these spheres originate? How are they derived from preexisting cells? We may answer this question in two ways. The protoplasm of the cell may assume throughout a uniformly homogeneous and more highly-refractive character; the cell, as a whole, being gradually transformed into a colloid sphere, in the interior of which, by the addition of appropriate reagents, we are able, for a time at least, to demonstrate the central nucleus. Or the colloid sphere may originate at one point in the protoplasm, near the nucleus, or, according to some authors, in the place of the nucleus. Small at first, it grows to a size so considerable that the residual portion of the cell is pushed aside, becoming, as it were, a mere appendage of the sphere. At this stage the cell tends to assume the form of a ring surrounding the sphere; of a signet ring when the still existing nucleus forms a projecting knob at one point in its circumference (cf. fig. 12).

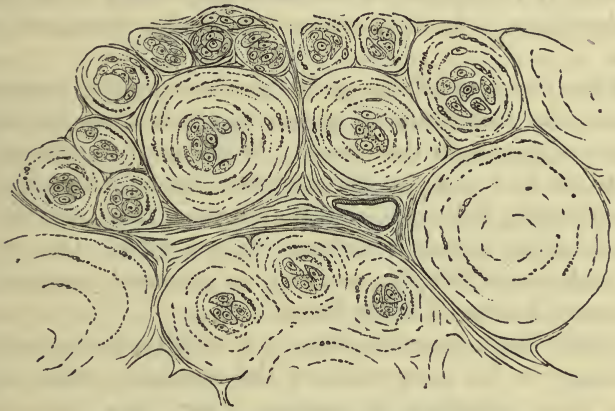
Finally, the colloid sphere escapes from its place of origin, leaving the remainder of the cell behind as a granular mass, which speedily crumbles away and disappears.

The colloid spheres, whatever their origin, continue for a time to grow, *i.e.* to swell (for they become less and less distinct in the process), until their refractive index equals that of the colloid mass already present, with which they may be said to blend in the strictest sense of the word.

As colloid matter, like mucus, is capable of swelling greatly by imbibition, the colloid metamorphosis becomes proportionately conspicuous to the naked eye. Little groups of from ten to twelve cells, which, before their metamorphosis, can hardly be said to exist for the unaided eye, are converted into a jelly-like particle, still very small, but quite visible, as we have already pointed out with reference to the cell groups of the *nucleus gelatinosus* after they have undergone colloid degeneration (§ 41). The greater the size of the particle the more marked is its amber tint, its transparency, and its tremulous, jelly-like quality. But these properties only last until the particle reaches a certain size, or, to speak more accurately, a certain stage of development. The substance then assumes more of a viscid character, and finally becomes quite fluid. The ultimate chemical product of colloid metamorphosis is, like that of mucous softening, sodic albuminate; its morphological result is either a single, smooth-walled cyst, or a complete system of intercommunicating cysts, the so-called "alveolar structure."

To understand this we must remember that in the pathological development of colloid matter (colloid cancer) a great number of colloid foci originate in close proximity to one another.

Fig. 13.



Section from a colloid or alveolar cancer, $\frac{1}{300}$.

The matrix of the connective tissue in which they originate suffices for a while to keep the individual colloid granules apart; but as their size increases, the partitions between them waste, the partial or complete fusion of neighbouring cavities resulting in an irregular, loculose subdivision of the disposable space, which may very fairly be compared to the alveolar structure of the pulmonary parenchyma (fig. 13). (Cf. the section on Colloid Cancer.)

3. Conditions of Infiltration.

§ 45. The degenerations which come under this head are less worthy to be called "retrograde metamorphoses" than those which we have hitherto discussed.

The affected structures retain their external form even in advanced stages of morbid change; they retain it, that is, to such an extent, that no question can arise as to the identity of parts in their unaltered and in their altered state; cells can still be recognised as cells, vessels as vessels, &c. In harmony with this is the fact, that they never entirely lose their physiological capacity, though in this respect the greatest differences exist; for while amyloid and calcareous deposits are associated with an impairment of functional power of the most extreme kind (amounting in some cases to a "vita minima"), pigmentary and fatty infiltration are borne with comparative ease. It cannot, however, be denied that a definite impairment of functional capacity, proportionate to the degree of the alteration, occurs in all cases, and this obliges us to reckon them among the retrograde processes.

All the members of the group have one leading feature in common—the abstraction of certain materials from the blood, and their deposition in the tissues. While other constituents of the nutrient fluid pass the cells and other structural elements by, without leaving any trace of their presence, these matters are retained, as the deposit is retained upon a filter. One of the main conditions of this phenomenon is an abnormal accumulation of the morbid material in the blood.

In many cases, therefore, there is a simultaneous or antecedent change in the composition of the circulating fluid, a dyscrasia, which manifests its presence, apart from the clinical phenomena of the constitutional disorder, by causing the anatomical lesions in question in the most various parts of the organism. This association with a dyscrasic condition of the blood may be recognised even in the histological details of the process; for the singular circumstance that the minute arteries and capillary vessels are the first to undergo infiltration does not admit, in my opinion, of being otherwise explained. It is here that the centrifugal current of nutrient fluid traverses the walls of the circulatory apparatus; and should the *plasma sanguinis* be loaded with a substance prone to become deposited in cells, connective tissues, and homogeneous membranes, the substance in question will have its first chance of being deposited, in the parietal elements of this section of the vascular apparatus.

Besides the antecedent dyscrasia, a great part in the etiology of these infiltrations is played by the local predisposition, the special state, and the individual peculiarities of the several tissues.

All the organs are not equally fitted for the reception of the peccant material, granting the existence of the dyscrasia. Suppose, for example, the blood to be loaded with an excess of fatty matter, we find the liver and the areolar tissue better adapted for its reception than any other part of the body. Suppose earthy salts to be present in the blood in excess, we find them to be deposited by preference in the lungs. Amyloid degeneration, too, invades the organs of the body in a definite order, the kidneys being first affected, then the spleen, liver, &c.

In conclusion, we must not omit to recognise the possible operation of purely local causes. These are especially traceable in the case of pigmentary metamorphosis, which is most frequently determined by local hyperæmia, hæmorrhage, and inflammation. A few, though certainly the most interesting and important varieties of pigmentation, depend on a constitutional disorder, as in the case of melanotic and melanæmic coloration, and the bronzed skin of Addison's disease.

In the course of the ensuing sections we shall often have occasion to refer, now to the local, now to the general, character of these "infiltrations;" the sole object of these preliminary remarks being to direct us to the position of these processes in the natural history of disease, and to establish the general characters of the group as a whole.

A. *Amyloid Infiltration.*

§ 46. Passing to the consideration of amyloid infiltration, lardaceous, waxy degeneration, glassy swelling (glasige Verquellung), we find ourselves at the outset in a predicament with regard to the definitions given above, inasmuch as we are unable to give a name to the substance contained in the blood, and which transudes from it into the tissues. The infiltrated matter, according to *Kekule's* analysis, is an albuminous body; one which differs, however, from fibrin, albumen, &c., by turning of a bluish-violet or red colour when acted upon by iodine. It most frequently assumes a reddish-brown or mahogany-red tint. This reaction, otherwise peculiar to the members of the amylaceous series, taken together with the circumstance that the substance in question is occasionally found to occur in concentric corpuscles, resembling those of vegetable starch, induced its discoverer, *Virchow*, to call it "amyloid." Now, if we search the blood, even in persons whose organs are most widely affected with waxy degeneration, for an albuminous substance yielding the same reaction, we shall search in vain. Indeed it is only from circumstantial evidence that we conclude that amyloid degeneration is a genuine infiltration.

Since amyloid matter is capable of being reddened by iodine only after it has left the blood, it is right that we should show by analogy that an albuminous body derived from the blood, and undoubtedly forming one of its constituents, may be converted into amyloid matter after it has left that fluid. I believe this problem to have met with a satisfactory solution by the inquiries of *Friedrich* and *Biermer*. Any one who has conducted experimental investigations on extravasated blood will at once admit, that the concentrically-laminated corpuscles found by these observers in hæmorrhagic deposits in the lungs, are formed by the deposition of fibrin round little clusters of blood corpuscles, shreds of tissue, carbonaceous particles, &c.* The fact that some of these corpuscles exhibit the iodine reaction, proves conclusively that here at least the fibrin of the blood must have been converted into amyloid matter. We must not jump forthwith to the conclusion, that impregnation with fibrin is the essential factor in amyloid infiltration. We need only assume that an albuminous constituent of the nutrient fluid may be arrested on its way through the tissues, and deposited in a solid form. As the chief property of fibrinogen is its persistent tendency to assume the solid state, this, more than any other of the albuminous constituents of the blood, will have a claim on our attention. Indeed, if we follow up the course of amyloid degeneration in each individual case, we shall find much in favour of this view; the question is not, however, so far advanced towards solution as to require further discussion in this place.

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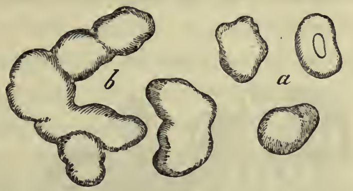
* Those interested in the pathological histology of the lungs, will find it instructive to bestow a passing glance at the forms exhibited by charcoal dust under the microscope. They will see particles which may very readily be mistaken for blood crystals, owing to their peculiar spiked outlines and their colour, which appears a transparent reddish brown in thin layers. Particles of charcoal are found in very many lungs; for their angular shape and pointed processes enable them, when introduced by the respiratory act, to penetrate more easily than other foreign bodies into the soft parenchyma of the lungs, where they remain fixed. The presence of circular perforations renders us absolutely certain about the carbonaceous nature of such pseudo-crystalline bodies; for these are the pores in the dotted cells of coniferous wood (*Virchow's Archiv,* x. Taf. iii. fig. 5).

§ 47. Let us glance at the histological phenomena of the process. The cell which has undergone amyloid infiltration differs from a normal cell—first, by its greater size. It exceeds the normal standard usually by one-third, sometimes by two-thirds, of its diameter; nay, its size may even have been doubled.

Fig. 14.



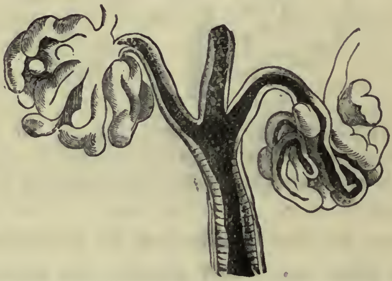
Liver-cells infiltrated with amyloid matter. *a.* Isolated cells; *b.* A fragment of the secreting network in which the boundaries of the individual cells have ceased to be visible.

This increase in size is attended by an alteration in shape; the cell grows fuller and more plump; its characteristic outline fades; its angles are blunted; the most striking feature, however, being its homogeneous, transparent, faintly opaline aspect. The nucleus ceases to be recognisable; everything points to a thorough impregnation of the protoplasm with a highly refracting substance, which masks all inequalities produced by minor differences of refractive power. When several amyloid cells are in contact with one another, they usually coalesce to form irregular and, for the most part, elongated masses, in which the lines of demarcation between the individual elements can no longer be discerned.

§ 48. Amyloid infiltration of the non-cellular elements of the tissues corresponds in every respect to that of the cells. The tumefaction, the amorphous and homogeneous, glassy transparency, are alike in both. This we may see in structureless membranes, intercellular and interstitial substances of all kinds. Were additional evidence needed in support of our proposition that amyloid degeneration is really an infiltration, we should find it in the uniformity of its effects on structures which are so far apart from one another in the histological series. But the view in question—a view which no one ventures to dispute—receives its most effectual support from a consideration of the course taken by the degenerative process in individual organs. I refer the reader to those sections of the Special Part, which treat of this matter, limiting myself here to a description of the change as it occurs in the vessels.

The fact that the minute arteries, with their arterioles (Uebergangsgefässe), and the capillaries, are a favourite, and usually the primary, seat of all infiltrations, has been already placed in its true light. Amyloid infiltration stands foremost in this respect.

Fig. 15.



Malpighian tuft infiltrated with amyloid matter (from the kidney), $\frac{1}{300}$.

In any organ it is the efferent vessels which are first affected. In these, the gradual progress of the infiltration from within outwards may readily be traced. At some points the intima alone, with its homogeneous limitary membrane, exhibits the glassy intumescence; at others, the muscular fibres are also implicated, and assume a peculiar homogeneous, glistening, somewhat blurred appearance; in extreme forms of the disease, such as those described by *Beckmann* in the thyroid body, the infiltration is found to extend to the adventitia and surrounding connective tissue.

The inevitable consequence of this degeneration is a proportionate narrowing of the calibre of the affected vessels.

Their lumina are obstructed by the swelling of their walls, and the obstruction may amount to absolute occlusion. Fig. 15 represents a Malpighian tuft of the kidney which has partially undergone amyloid degeneration; it shows how the blue injection (and consequently the blood during life), penetrates into those capillary loops only, which do not present the characteristic homogeneous and glassy appearance. The addition of iodine produces an exquisite alternation of red and blue loops in the rete mirabile.

§ 49. In this degeneration of the vessels, we find the principal cause of those abnormalities which amyloid organs exhibit to the naked eye.

The most marked of these is the comparative bloodlessness of the organs. This anæmia is not due solely to the closure of the vessels by swelling of their walls; it is partly accounted for by the greater relative space occupied by the degenerated as compared with the normal parenchyma, and the consequent compression of the vessels; that this is so, is proved by the case of amyloid infiltration of the liver. In this organ the amyloid matter is chiefly deposited, not in the capillary walls, but in the hepatic cells which lie between them; and yet the anæmic condition of the waxy liver is as distinct as possible.

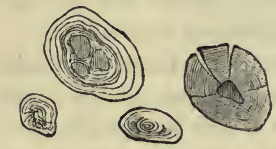
The less the colour of an organ depends on the blood which it contains, the more apparent is the special colour of the organ itself. This is especially true of organs which have undergone amyloid degeneration; in them we see the peculiar colour and quality (Beschaffenheit) of the amyloid matter asserting itself in proportion to the degree of the infiltration. The parts assume a pale yellow or clear grey tint; they become as soft as wax, the pressure of the finger leaving a persistent mark. When the degeneration is absolutely complete (a very rare phenomenon, which has hitherto been observed only in parts of the thyroid gland and the spleen), the comparison with white wax, proposed by *Virchow*, is most appropriate.

§ 50. The form of amyloid degeneration described above commonly follows prolonged suppuration in bone, caries of vertebræ, necrosis, &c.; it is not unfrequently associated, moreover, with constitutional syphilis, more rarely with pulmonary tuberculosis and other cachexiæ; all cases in which a pre-existent dyscrasia of the blood may be unconditionally assumed as its basis.

I have only a few words to add with reference to the *local* occurrence of amyloid matter. Allusion has already been made to the laminated concretions found in hæmorrhagic deposits in the lungs. We saw that fibrin, after lying for some length of time outside the current of the blood, became susceptible of reacting to iodine; now it appears that other albuminates and albuminoid matters are capable of undergoing a similar change. The laminated concretions which are always present in the follicles of the prostate gland of adults, exemplify the possibility of an albuminous body being deposited in a solid state from the secretion (mucous or colloid?) of a gland, round isolated cells, or groups of cells, and of its subsequently, though not invariably, becoming susceptible of coloration by iodine, the colour inclining usually rather to blue or violet than to red.

By the concentric addition of similar matter these bodies may reach a considerable size; two or more may become invested by a common capsule, in which case they may be recognised by the naked eye, and their behaviour with iodine tested.

FIG. 16.



Laminated concretions of amyloid matter from the efferent ducts of the prostate.

The concentrically laminated corpuscles which are normally present in the ependyma of the cerebral ventricles, and which occur in enormous numbers in the so-called grey atrophy of nerve tissue, have given rise to much discussion; their significance is purely local. It is still undecided whether they are to be regarded as cells infiltrated with amyloid matter, or as concretions; their remarkable uniformity of size, and their not wholly irregular distribution in the ventricular ependyma, are more in favour of the former than the latter supposition.

With iodine they assume a pale blue tint, which passes into violet on the addition of sulphuric acid.

B. *Calcification.*

Calcification plays a less important part in pathology than amyloid degeneration. It denotes the infiltration of tissues with calcic phosphate and carbonate in a solid form. The most gigantic physiological prototype of this process—one, however, which exhibits many peculiar features—is the deposition of calcareous salts in the matrix of bone. On the other hand, it must be carefully distinguished from all crystalline deposits from the secretions, as *e.g.* those occurring as sediments and incrustations in the urinary passages.

Before considering the phenomena of calcareous infiltration, we must settle a question, on the due answering of which so much depends, that it may justly be regarded as fundamental. How are calcic phosphate and carbonate held in solution by the blood and the juices of the parenchyma? and what may we regard as the probable conditions which determine their precipitation in the tissues?

Our answer to this question is fragmentary. From the intimate combination of minute quantities of calcic phosphate with all the albuminates (the salt remaining after their calcination as a residual ash), we may infer that it is chemically bound up with albuminates in all the nutrient fluids of the animal organism, and that, when so combined, it is soluble in water (*Gorup-Besanez*). Apart from this hypothesis we have the significant fact that calcic phosphate, and still more, calcic carbonate, are soluble in liquids containing free carbonic acid. The blood and nutrient fluids of the organism fulfil this condition. Hence it is, to say the least, not improbable that free carbonic acid is an important, perhaps the most important, agent in the solution of the earthy salts.

Unsatisfactory as it is to have to give a hypothetical answer to the first part of the question, we find ourselves in a far more puzzling predicament when we attempt to give an adequate explanation of the causes which determine the precipitation of these salts. But the attempt must nevertheless be made. The roundabout but only effective way to get at a solution of the problem is to consider all the known examples of calcification one by one, with a view to finding out what the various localities in which we find calcium salts precipitated have in common; and, further, how this common property adapts them for becoming depositaries of these salts. We must be careful to eliminate all those cases of calcareous infiltration in which a simultaneous reabsorption of calcium salts from the osseous system is taking place, and in which, therefore, we are led to infer with certainty that the blood is saturated with them, that there is a true "calcic dyscrasia." Such cases must be excluded, inasmuch as it is obvious that, the blood being capable of holding only a limited proportion of calcium salts in solution, precipitation must ensue at some point or other, after the limit of saturation has been reached. We must confine ourselves to the consideration of calcareous infiltrations of a purely local character, beginning with physiological examples of the process.

§ 52. TRUE BONE TISSUE originates as follows:—In a connective tissue, richly provided with capillaries, which map it out into vascular territories or islets of parenchyma, a compact matrix is developed; it first appears in the centre of each territory; at the point, therefore, which is farthest from the blood-current. The cells, which are already assuming a stellate form, become enclosed in this matrix at regular intervals, the matrix itself undergoing impregnation with earthy salts. This typical series of phenomena underlies all ossification, whether in membrane or in cartilage. In either case the medullary spaces are first sketched out in this way. The regular repetition of this sequence of matrix-formation, enclosure of cells and calcification, leads on the one hand, to the production of compact bone tissue disposed in concentric laminæ round the blood-vessels; while, on the other, it narrows the original medullary cavity to the size of a Haversian canal. For the details of the process I refer the reader to textbooks of normal histology. For us the important point is that the earthy salts are first deposited along those neutral lines which may be looked upon with equal justice as the limitary or the axial lines of the vascular territories. It need hardly be said that these lines cross each other at certain points, and must therefore form a network resembling that formed by the capillaries themselves; this inference being fully corroborated by the examination of an osteophyte at an early stage of its growth, or of a cylindrical bone at its ossifying border, where it adjoins the cartilage.* We cannot but recollect that in the parenchyma of other connective tissues the lymphatics stand very constantly in a similar relation to the capillaries. I pointed out, as early as the year 1859,† that the lymphatics in the tail of the tadpole were invariably situated in those parts of the parenchyma which were farthest from the vessels. Since that time the course of the capillary lymphatics has been repeatedly investigated, and the above statement has been again and again confirmed. (Cf. *Von Recklinghausen*, "The Lymphatics and their Relation to the Connective Tissue," Plate I. fig. 1.) This arrangement is quite in harmony with the function of the lymphatics as drains for the removal of superfluous pabulum; those points of the parenchyma towards which the currents proceeding in every direction from the capillaries converge, being furnished with adequate means of drainage. I will show hereafter how this digression may be brought to bear on the subject now in hand; at present I will only say that true bone is one of the few tissues which are absolutely devoid of lymphatics.

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* *See* "Osseous System," Exostosis.

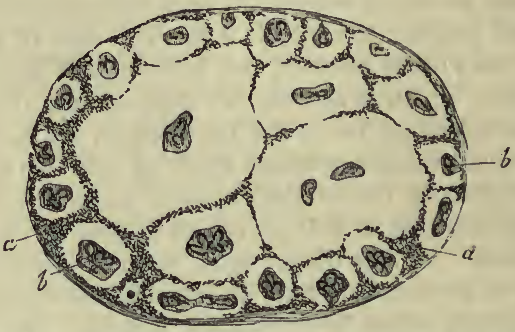
† *De Vasorum Genesi.* Inaugural Dissertation. Berlin.

Just as the limits of the individual vascular territories of the young bone are marked out by calcareous infiltration, so the bone, as a whole, is separated from the cartilage by a limitary zone of tissue infiltrated with earthy salts, belonging half to the cartilage and half to the bone; it is this very zone of calcification which has so long obscured our knowledge of the development of bone. In strict accuracy we must consider this neutral boundary as belonging, not to the bone proper, but to the sum of the outermost medullary spaces which lie next the cartilage, and are supplied by the terminal loops of the nutrient artery. This is distinctly seen in that perversion of growth which constitutes rickets. In this disease some of the terminal medullary spaces of the bone penetrate far into the proliferating layer of the cartilage, which is of unusual breadth. The zone of calcification is interrupted at many points; and even *Virchow* remarked that to make up for this, little centres of calcification are met with higher up in the substance of the cartilage, which may be viewed as in some sort the *membra disjecta* of the calcareous zone. On making a transverse section through this region, we may see how the entire mass of cartilage is partitioned out into oval territories of unequal size by the said infiltration of earthy salts, the middle of each territory being occupied by one of the projecting medullary spaces alluded to above, with its axial capillary loop. Here too, therefore, we find the calcareous infiltration mapping out the vascular territories, and that in a tissue which possesses no trace of lymphatics either in these "lines of contact" or in any other part of its substance (fig. 17).

I consider myself fully justified in expressing the view, founded on the above data derived from normal histology, that peculiarities in the movement of the nutrient juices, and especially a certain retardation, or even stagnation, of their current, which may be assumed as likely in the said localities, owing to the absence of lymphatics, stand in some sort of causal relation to the process of calcification. Should this view be correct, we might conceive the precipitation of the earthy salts to occur in some way like this: the free carbonic acid, to which their solubility is due, in consequence of its great diffusive power, forsakes the stagnant nutrient fluid, and escapes from the organism by other channels; while the calcareous salts, rendered insoluble by its removal, are forthwith deposited in a solid form.

§ 53. Passing next to PATHOLOGICAL CALCIFICATION, we find it occurring chiefly as a secondary phenomenon, as a consequence of inflammation and morbid growth. The earthy matter is deposited either in the newly-formed tissues themselves, or in the residual parts of the diseased organ, which are surrounded and permeated by the products of inflammation and morbid growth. To what extent we may be justified in assuming a disturbance in the circulation of nutrient juices as the efficient cause of the precipitation of the earthy salts in each single case, we shall see when we consider them individually. Calcification may occur in various tissues; in the connective tissues, in vessels, in cellular and glandular tissues, in muscle, both striped and unstriped, but oftenest in cartilage, the pathological coinciding here with the physiological order. The cartilages of the larynx and trachea are often found calcified, as a result of chronic catarrh of the respiratory mucous membrane; the intervertebral substances, in consequence of chronic suppurative caries of the vertebræ; the costal cartilages of old people are often affected

FIG. 17.



Calcification of cartilage. Transverse section through the zone of proliferation in the epiphysal cartilage of a rachitic subject, $\frac{1}{10}$.

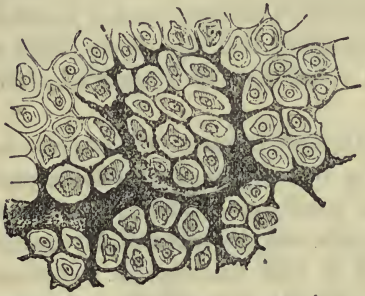
in this way; finally, we often find those small globular portions of cartilage, with which we are familiar, on the one hand as constituent elements of enchondromata, on the other as outgrowths from articular cartilages and synovial membranes, impregnated with earthy salts. In every one of these cases the calcareous deposit first appears in the central parts of the cartilaginous structure, in those which are farthest from the surface, where the circulation of nutrient fluid is most hindered, perhaps even totally arrested. Provisionally, therefore, we are justified, on pathological grounds, in assuming that the precipitation of calcareous salts results from a retardation or stagnation of the nutrient fluid.

§ 54. In studying the HISTOLOGICAL DETAILS of calcareous infiltration, we will avail ourselves first of the admirable example afforded by the development of cartilage. Cartilage is a connective substance, made up of cells and an intercellular matrix. We cannot as yet tell why it is that calcification sometimes begins in the cells, sometimes in the intercellular substance. Suffice it to say that either may be first affected; indeed, it is characteristic of this, as of other forms of infiltration, that the most diverse structural elements are liable to be involved.

The first visible effects of calcification are the so-called *earthy granules* (Kalkkrümel) small, roundish or angular particles, which appear black by transmitted, white and glistening by reflected light, and which are imbedded more or less thickly in that part of the cartilage (say its matrix) which is primarily involved. Attempts have been made to show that these particles are actually the earthy salts, and to demonstrate crystalline form in them; this, however, was a mistake. The earthy granules may, indeed, owe their leading properties, their density, their whiteness and opacity to the calcareous salts with which they are impregnated; nevertheless we must distinguish in every granule—first, a particle of the matrix of equivalent size; and, secondly, the earthy salts which it contains. Without this distinction, or rather generalisation, the subsequent changes would be not merely inexplicable, but utterly impossible; for after the matrix has first of all been darkened by the calcareous granules, it assumes in the sequel a homogeneous lustre, such as we find in the matrix of bone, this appearance being clearly due to the mutual approximation of the calcareous granules, and their ultimate coalescence, when they can no longer be individually distinguished. Now, since the matrix retains its former bulk after calcification is completed, it is clear that the earthy salts cannot have been superadded to its proper substance in particles as large as the granules in question; hence we are compelled to assume that each granule is made up of matrix *plus* earthy salts.

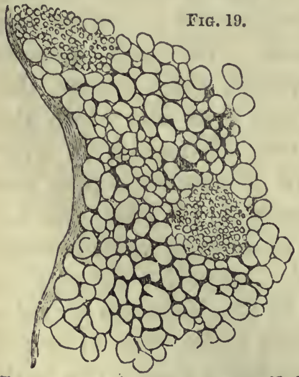
So long as calcification does not extend beyond the matrix, the appearance presented to us is that of a white and glistening reticulated network, whose tenuity is proportionate to the amount of space occupied by the cells and the consequent width of the intervening trabeculæ of intercellular substance (fig. 18). *Rokitanski* describes, in addition, a segmentation of the matrix into spheroidal masses, which is especially frequent in the fibro-cartilages and in enchondromata. My own observations confirm his statements. The appearances in question must not be confounded with those presented by the earthy granules. *Rokitanski* very justly compares them with the calcification of fibrillated intercellular substances.*

Fig. 18.



Calcification of cartilage. Transverse section through a loose cartilage of the elbow joint, $\frac{1}{300}$.

Fig. 19.



Transverse section through an ossified pleuritic false membrane (after *Rokitanski*).

* This appearance of spheroidal segmentation is beautifully exemplified in the calcification of tendons, where it has been most elaborately investigated by *Lieberkühn* (*Reichert* und *Dubois*, Archiv, 1860, No. 6, p. 824 *seqq.*). Between the discoidal figures presented by the fibrillæ in transverse section, interstices of variable size are occasionally seen; these are often deceptively like bone corpuscles, on account of their jagged and excavated margins. A little thought is enough to convince us, without our having to recur to longitudinal sections for aid, that we have to do, not with independent elements, but with appearances due entirely

The globular, or rather discoidal, masses are the calcified fibrillæ seen in transverse section. There is nothing strange, therefore, in our meeting with this spheroidal segmentation of the calcified matrix in fibro-cartilaginous structures; and we have already seen, when considering the phenomena of softening, that the matrix of hyaline cartilage is also liable, under certain conditions, to break up into fibrillæ.

The calcification of cartilage, when the cells are primarily affected, gives rise to optical results of a very different order. In this case a peculiar thickening of the cartilage capsules (sclerosis, *Virchow*) precedes all further changes. The thickened capsule takes up the earthy salts; sometimes, and indeed usually, as a cloud of earthy granules; occasionally, however (as was first observed by *Kölliker* in rickets), the calcareous impregnation gradually leads only to a whitish opalescence by reflected light, while the structure *never loses its transparency.* It is this latter circumstance which has enabled us to ascertain that the entire series of these changes takes place without involving the proper substance of the cells. From first to last the process is exclusively capsular. The capsule continues to grow thicker at the expense of its cavity. The size of the original cartilage cavity, therefore, undergoes progressive contraction, the capsule loses its spheroidal form; for, as the thickening of the capsule does not proceed uniformly at all points, little funnel-shaped gaps being left at regular intervals (analogous to the pores of vegetable cells during their conversion into wood), the cell-containing cavity ultimately assumes a stellate, jagged outline, singularly like that of a lacuna of bone. Should the matrix attain the glassy and transparent stage of its calcification, either simultaneously or subsequently, we may fairly speak of a direct ossification of hyaline cartilage. Such *false bone,* which stands towards true bone in the same relation (§ 52) as other calcified connective tissues, such as tendons, fasciæ, coats of vessels, &c., is not common; it always occurs in small bits; we find such bits in enchondromata, and in the spongy substance of ricketty

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to the contact of adjacent circles; for we see them varying in size and shape within the widest possible extremes. (*See* the annexed drawing of a transverse section through an ossified pleuritic false membrane.)

bones, where they are, so to say, inlaid near the ossifying border of the cartilage.

So much for the histological details of calcification as it occurs in cartilage. Its individual features recur in the most various tissues. In order not to anticipate the special descriptions contained in the second part of the present work, we must content ourselves here with the remark that calcification, wherever it occurs, is always a true infiltration. The specific form of the infiltrated structures, at least in its coarser outlines, is never effaced. We are able, as a rule, to restore matters to their previous condition by simply removing the earthy salts with hydrochloric acid.

c. *Pigmentation.*

§ 55. Pigmentation (chromatosis) is one of the most interesting subjects in pathological histology. Its limits are not very well defined.* I must premise therefore, that I do not intend, under the head of Pigmentation, to discuss every change of colour which may occasionally be exhibited by diseased parts, but to confine my attention to those positive colorations which are due to the infiltration of some pigmentary substance into the tissues. Red, yellow, brown, and black pigmentary particles, with every imaginable intermediate tint, may be met with as infiltrations. They are all, however, ultimately derived from one and the same source—the hæmatin of the red blood-corpuscles.

We are not fully acquainted with the chemical composition of hæmatin; we do not know how it is produced. Itself, in all probability, an albuminous body, it is intimately combined in the red corpuscles with another albuminous substance which is destitute of colour (*globulin*). This compound, under certain conditions, crystallises in long red needles (*hæmato-crystallin*). To understand how yellow, brown, and black pigments may be derived from the colouring-matter of the blood, we must first glance at the physiological metamorphoses to which this substance is liable. The most important of these, and in some sense typical of all the rest, is its transformation into bile-pigment. This phenomenon, however plausible *a priori*, has long been shrouded in mystery. It seemed hazardous, and very justly so, to derive a chemical substance produced exclusively by the activity of the hepatic cells, from a certain constituent of the blood, solely on the ground of its possessing like optical properties. At the present day these scruples have lost all meaning, and that mainly in consequence of the following observations. In places where blood has some time previously been extravasated, hæmatoidin is not unfrequently found in the form of small, fiery-red crystals, belonging to the rhombic system (fig. 20). There can be no doubt that this hæmatoidin is derived from the blood-pigment; and yet it differs from hæmatin in containing no iron. When treated with powerful oxidising agents, such as concentrated sulphuric acid, it gives a play of prismatic colours. It need hardly be said that these very properties by which hæmatoidin is distinguished from the colouring matter of the blood, bring it nearer to bile-pigment. This alone made it highly probable that bile-pigment ought to be regarded as derived from the colouring matter of the blood; and this probability became a certainty when *Valentiner* discovered that hæmatoidin could be extracted from dried and powdered bile by means of chloroform. Now, it is quite true that a crystalline pigment may be obtained in this manner, not distinguishable at first sight from hæmatoidin. Nevertheless *Valentiner's* discovery had to submit to a slight correction. *Städeler* found that the crystalline colouring matter of the bile (bilirubin, $C_{32}H_{18}N_2O_6$) differed from hæmatoidin ($C_{30}H_{18}N_2O_6$, *Robin*), not only by a trifling variation in the angular measurement of its crystals, but also in containing two atoms more carbon. *Städeler*, however, considers this difference as too insignificant to shake the proposition that bile-pigment is derived from blood-pigment. The red corpuscles, as they grow old, part with their colouring-matter to the serum; from this it is taken up by the liver-cells, which transform it into bile-pigment; as such it is ultimately excreted in the fæces. Before it is

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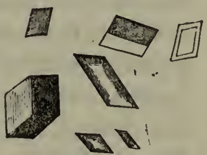
* For example, all those tissue-changes which have already been described, cause some peculiar coloration or decolorisation of the affected structures. So too, desiccation, shrivelling, condensation may all modify the refractive index, and so alter the optical properties of the tissues.

FIG. 20.



Crystals of Hæmatoidin (after *Virchow*).

thus removed, when retained in the gall-bladder for any length of time, it undergoes further changes, passing through shades of yellow, grey, brown, and black, which *Städeler* terms respectively *bilifuscin* ($C_{32}H_{20}N_2O_8$), *biliverdin* ($C_{32}H_{20}N_2O_{10}$), *biliprasin* ($C_{32}H_{22}N_2O_{12}$) and *bilihumin*; bilifuscin differing from bilirubin in containing two atoms more HO, biliverdin from bilifuscin in containing two atoms more O, biliprasin from biliverdin, again, by an access of 2 HO, whilst bilihumin is a black, insoluble, very highly oxidised substance.

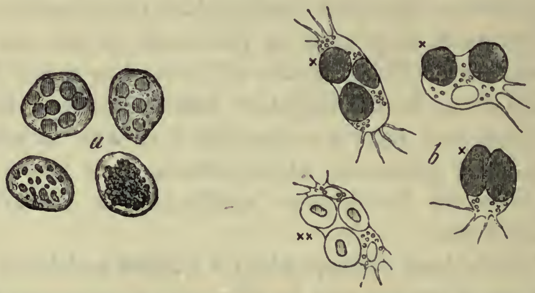
§ 56. The scale of colours enumerated above serves, as already stated, as a standard for the course of all other chromatoses, whether physiological or pathological. The former, to which I can only allude by the way, are due to the fact that certain other cells either possess, like those of the liver, or obtain with the lapse of years the power of appropriating the blood-pigment dissolved in the serum, and of condensing it in their interior; among these may be enumerated the epithelial cells of the choroid and the rete Malpighii, and certain ganglion-cells. The black pigment found in the lungs deserves to be considered separately. I have already called attention (in a note to § 46) to the ease with which particles of vegetable charcoal (especially wood charcoal) become imbedded in the lungs, where they may be mistaken for pigment-granules. Hence I am not disposed to deny that a certain small proportion of the lung-pigment may be due to the accidental admission of carbonaceous particles. The probability of this is enhanced by the obstinate resistance which the pulmonary pigment offers to the action of reducing agents, a fact which leads us to infer that it must, at all events, contain a very large proportion of pure carbon. Moreover, the observation that the pigmentary particles of the lungs are occasionally found enclosed in cells can no longer be held to invalidate the coal-dust theory, inasmuch as it has recently been demonstrated that cells of soft consistency, *e.g.* colourless blood-corpuscles, may take up minute particles of solid matter into their protoplasm. Notwithstanding all this, however, it is only a small proportion of the lung-pigment which can be regarded as consisting of charcoal particles introduced from without, the remaining part being unquestionably derived from the colouring-matter of the blood. The proof of this is to be found, on the one hand, in the anatomical similarity between this and other forms of pigmentation; on the other, in the fact that a pathological excess of pigment in the lungs is met with under those very conditions of hyperæmia and hæmorrhage which cause a deposit of pigment in other organs. It may plausibly be imagined, moreover, that the blood-pigment, in a locality where the osmotic interchange of gases is so extraordinarily active, may be converted by an imperfect process of combustion into animal charcoal more speedily than elsewhere.

§ 57. Turning our attention to pathological chromatoses, we find, as was hinted in our introductory remarks, that the great majority of these are due to local disturbances in the circulation. They are singularly persistent; they serve, accordingly, as evidence not only of existing congestions, but of former hyperæmic states of this or that organ, or part of an organ. It is hardly necessary to add that not every hyperæmia is followed by a deposit of pigment; nay, we may almost consider it a rule that only those congestions, during which extravasation of blood, or its permanent stagnation in the vessels occurs, are followed by pigmentation. This assertion will seem less rash if we reflect that apart from hæmorrhages of notable amount, both acute inflammation and passive congestion give rise to minute but proportionately numerous extravasations from the capillaries. But it relies for its ultimate justification on the evidence of anatomical facts.

All purely local pigmentations, *i.e.* those which are not connected with dyscrasiæ, may be shown to originate in the absolute stagnation of variable quantities of blood; sometimes of only a few blood-corpuscles which have not even succeeded in completing their escape from the vessel, but have stuck in the *tunica adventitia;* more frequently of little streaks and drops of blood, or even larger collections, which lie in the parenchyma outside the vessel. We need not enter into the manifold changes to which such stagnant portions of blood are liable (organisation, suppuration, &c.); we may confine ourselves to an observation, which is of the utmost moment as regards the production of pigment, viz. that the red discs generally lose their colouring-matter, which is thus at the disposal of the neighbouring tissues in a state of solution. We had the opportunity of becoming acquainted with a process not unlike this during the putrefaction of the blood. It follows accordingly that decolorisation is a phenomenon not only associated with the sudden death of the blood-corpuscles, but serving also to usher in those changes which, as in the present instance, lead rather to a gradual dissolution, or to a prolonged existence in another form.

Note.—It is convenient to say a few words here about the conversion of the colouring-matter of the blood into pigment-granules without its previous escape from the corpuscles. I allude to the so-called "blood-corpuscle-holding cells." The mode of origin of these large, more or less round, bodies, consisting of several red blood-corpuscles imbedded in a colourless and homogeneous matrix (fig. 21*a*), was more important formerly than it is now. It was thought to support the theory of endogenous cell-development. Its histogenetic interest has now quite faded. It appears that these bodies are not always produced in the same way. I have convinced myself that in the stagnant blood of amphibia agglomerations of red and colourless blood-corpuscles (or such as have become colourless), exhibit all the appearances of the "blood-corpuscle-holding cells" (fig. 21*b*).

Fig. 21.



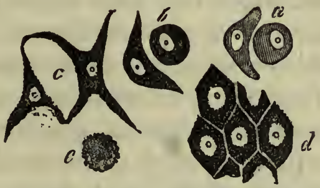
Blood-corpuscle-holding cells. *a*. Human; *b*. In frogs' blood, $\frac{1}{300}$.

Preyer states ("On Amœboid Blood-Corpuscles," *Virchow's* Archiv, xxx. 417), that similar optical appearances may be produced by the escape of the red contents of the corpuscles in stagnant frogs' blood in the form of drops of varying dimensions, and the subsequent incorporation of these drops into neighbouring amœboid cells after the manner of particles of cinnabar, or other solid granules of any sort. This theory admits of only a limited application to the "blood-corpuscle-holding cells" of mammals, since in them the blood-corpuscles occupy a more central position, and are enclosed on every side by a homogeneous border. Here I believe that we have no alternative but to assume that a layer of fibrin has been secondarily deposited round a group of blood-corpuscles. The phenomenon would thus correspond on a very small scale with that which recurs on a scale of ever-increasing greatness in all circumscribed hæmorrhages. The red blood-corpuscles go through their subsequent metamorphoses in the interior of this capsule, they lose their circular outline, grow darker, and finally run together to form a dark-brown or black pigmentary deposit.

§ 58. After the colouring-matter has escaped from the blood-corpuscles, and has permeated the surrounding tissues, we notice that their elements vary in their capacity for taking up the pigment which is thus presented to them. We remark preferences quite as decided as those which are manifested during the soaking of dead tissues in an ammoniacal solution of carmine. The cells attract the pigment more powerfully than the intercellular substances, homogeneous membranes, elastic fibres, &c. The cells therefore appear, even at this stage of the process, to be most intensely stained of a yellow or brown colour. But the coloration with hæmatin differs from staining with carmine, in that the nucleus does not exhibit a greater attraction for the pigment than the remaining portion of the cell. On the contrary, the nuclei are remarkable for taking no part in the change, appearing at a later period as colourless discs in the interior of the tinted protoplasm.

The stage of diffuse imbibition is followed by the precipitation of the pigment in a granular or crystalline form. This, too, we had occasion to observe during mortification. Hence, as also because it occurs not only *in* the tissue-elements themselves, but in the free fluid *between* them as well, we are justified in viewing it as a purely chemical phenomenon, having no connexion with the vital properties of the part. True that the crystalline deposits (hæmatoidin), which are least likely to depend on the action of the cells, are more frequent in the free fluid than in the interior of the cells; still, coloured crystals have also been detected in

FIG. 22.



Cells in various stages of pigmentary infiltration; (*a*, *b*, *c*, *e*), from a melanotic cancer; *d*, Pigmented epithelium from the vessels (same specimen), $\frac{1}{300}$.

the cells; moreover, the granular variety of pigment—which, we may remark by the way, is much the more usual form, crystals of hæmatoidin ranking among curiosities—is equally abundant within and around the cells. It consists, as the name shows, of minute yellow, brown, or black (melanin) granules, collected into little groups, which may unite under certain conditions to form larger masses of a more homogeneous character. Should they be numerous enough to fill the protoplasm of a cell, the colourless nucleus is partly pushed aside, partly surrounded; the pigmented cell appearing to be perforated by a circular gap or hole. Flat cells (choroid coat of the eye), in which the nucleus is in contact with both surfaces at once, retain their characteristic aspect. In spheroidal cells, however, the nucleus ultimately disappears, leaving a coloured corpuscle, in which only the external form of the cell can still be recognised.

§ 59. It is very unlikely that the functions of the cells are much impaired by pigmentary infiltration, for we find partial infiltrations of this nature in many of the most vitally important elements of the organism. I refer particularly to certain groups of motor ganglion-cells in the crura cerebri, whose constant impregnation with pigment has led to that region being designated as *substantia nigra vel ferruginea.* In the majority of local pigmentations, however, this question admits of no solution; for we cannot distinguish the functional troubles due to pigmentary infiltration from those which may have resulted from the antecedent local disorder. The opportunities afforded by certain pigmentary infiltrations originating in dyscrasiæ are much more favourable for this inquiry. I do not refer to melanæmia, which only deserves the name of a dyscrasia, inasmuch as a black pigment of local origin (in the spleen), enters the blood, and remains an abnormal constituent of this fluid during a certain time. When the deposit of this pigment in the capillaries of the brain gives rise to serious functional disturbances, these differ in no respect from such as might be produced by plugging of these vessels from any cause whatever; they cannot, therefore, be ascribed to the pigment as such. So too, the quantitative excess of colour in the skin, which *Addison* ascribes to a disease of the supra-renal bodies, is ill-adapted for our present purpose, owing to the obscurity which still hangs over the entire process. On the other hand, the history of melanotic sarcoma (*see* Morbid

Growths) shows us that a morbid state of the blood may exist, in consequence of which cell-growth, on a large scale, may take place in the most various regions of the body, the newly-formed cells being wholly or partially filled with granular pigment of a brown or black hue. The mechanism of this coloration is the same as that of the cells of the rete Malpighii, choroidal epithelium, &c. Indeed, the primary tumour is usually developed in the choroid or the skin. The cells get their pigment from that which is diffused throughout the nutrient fluid, and also, according to *O. Weber*, from capillary extravasations which may concur with the other changes. Be this as it may, the progress of the pigmentation, after the stage of diffuse imbibition, is the same here as elsewhere. The pigment is condensed and precipitated. The colourless sarcoma-cells are converted into pigmented sarcoma-cells. No one will deny that these pigmented sarcoma-cells retain their most destructive vital properties, and make use of them against the organism.

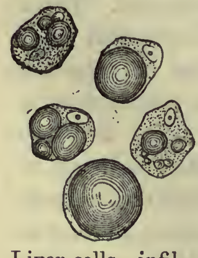
I do not believe that we are justified in speaking of a pigmentary metamorphosis in the same sense as of a fatty metamorphosis. For even though we may find in the juice scraped from melanotic tumours minute particles of pigment in countless numbers, together with cells in which the pigment-granules may be seen to exhibit dancing movements, and from which they may be seen to escape under our very eyes, yet we are not justified in inferring anything beyond an accident such as ultimately befalls all sarcoma-cells; moreover the numerous oil-globules which are scattered among the pigment-granules, but which are not easily to be distinguished from them, render it probable that we have really to do with a fatty metamorphosis.

§ 60. Besides hæmatin we must include the colouring-matter of the bile among the sources of abnormal pigmentation. If we were justified in assuming the derivation of bile-pigment from the colouring-matter of the blood, then biliary may be regarded as a mere variety of hæmic pigmentation. It is met with only in those organs which produce and excrete the bile. Suppose for a moment, that jaundice (icterus) is a pigmentary infiltration. In jaundice the bile-pigment, together with the other constituents of the secretion, is reabsorbed into the blood: hence, as long as the condition lasts, all the tissues of the body which are within reach of the nutritive fluid assume a yellow hue. Never, or only in very rare cases, is the biliary pigment deposited in a solid form; the pigmentary imbibition does not become a pigmentary infiltration. The latter, as has been already stated, occurs only in the liver and the bile-ducts. *Virchow* detected crystalline deposits of bilifulvin in the epithelium of the gall-bladder; granular pigment, of a yellow, brown, and especially of a black colour, is met with in the hepatic cells, not only in cases where the escape of the bile is hindered, but also in cases of obstruction to the return of blood from the hepatic veins. Here too we may have a coincident atrophy of the pigmented cells; but we must beware of regarding the pigmentary infiltration as the cause of the atrophy. This will become clear hereafter from the history of the pigmented nutmeg-liver, cirrhosis, &c.

D. *Fatty Infiltration.*

§ 61. The last member of the present series, and of the passive tissue-changes in general, is FATTY INFILTRATION. This must not be confounded with that fatty metamorphosis which has already been treated among the conditions of involution. There the oil-globules were but the forerunners of imminent dissolution; here they are, at worst, but a superfluous constituent of the cell; there they appeared as a product of the decomposition of the body of the cell; here they are brought to the cell from without, and retained in its protoplasm. Hence too, the anatomical appearances presented by fatty infiltration differ wholly from those due to fatty metamorphosis. They agree in this alone—that minute oil-globules make their appearance in the interior of the protoplasm. While, however, in the case of fatty metamorphosis these oil-globules continue to increase in number, without ever uniting to form larger drops, fatty infiltration mimics the development of real fat-cells (figs. 23 and 24). We rarely see more than two or three separate oil-globules in any one cell, and even these hasten—if the phrase may be allowed—to run together, so as to form a single large drop. The protoplasm, together with the

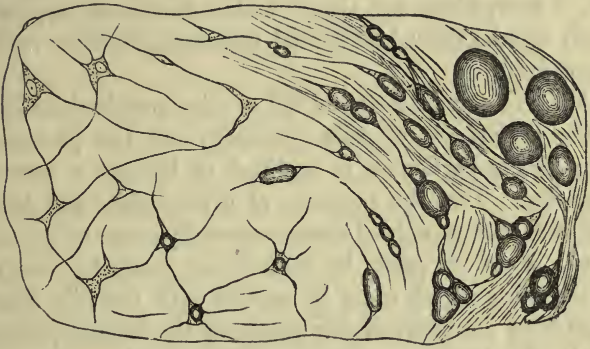
FIG. 23.



Liver-cells, infiltrated with oil, $\frac{1}{300}$.

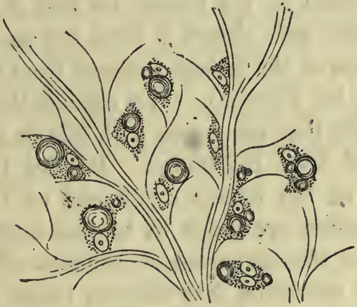
nucleus, is pushed to one side, just as in colloid degeneration. The larger the size attained by the oil-globule (and in the cells of a lipomatous tumour its size is often great) the more difficult does it become to realise the presence of any residue of protoplasm and nucleus. Nevertheless their existence is never to be doubted; for should the fatty matter be reabsorbed the nuclei invariably reappear (fig. 25).

FIG. 24.



Fatty infiltration of connective tissue, $\frac{1}{300}$.

FIG. 25.



Atrophied adipose tissue.

Neither are we justified in supposing that the functional activity of the infiltrated cells is wholly abolished. We know that a liver, every cell of which has undergone the alteration in question, is still capable of secreting bile, though the secretion is neither abundant nor concentrated, nor yet as brown in colour as it should be. The function of the organ is impaired, but not even in the most extreme degrees of the disorder is it wholly abolished. It need hardly be added that after the removal of the infiltrated substance, a removal which, as has been already stated, is everywhere and always within the bounds of possibility, the cells resume their interrupted functions, together with their previous form.

§ 62. We cannot certainly tell to what peculiarities it is due that the protoplasm of cells generally, and the protoplasm of certain cells in particular, is qualified to become a reservoir of oily matter. That the presence of glycocholate and taurocholate of soda renders animal tissues especially prone to be infiltrated with oil, is proved partly by experiment, partly by observation; since the parts which come in contact with the bile during its passage from the intercellular canals of the hepatic parenchyma to the large intestine, constantly exhibit the phenomena of fatty infiltration.

But contact with bile can only be considered as one of the factors in causing the infiltration. A second condition is that fatty matter in a finely-divided state should be readily accessible in the neighbourhood of the tissue to be infiltrated. The source of this fatty matter is a question of vital moment for the economy of the organism as a whole, but it is unimportant as regards the process itself. Thus in the bowel, we find it supplied by the chyme; the hepatic cells absorb it from the serum of the blood, and the epithelium of the biliary passages from the bile itself (as has been shown by *Virchow*). We cannot, therefore, entertain the slightest doubt that saturation with bile is a powerful determining cause of fatty infiltration. Besides the hepatic cells, the epithelium of the biliary ducts and of the bowel, other cells in the organism are liable to become infiltrated; foremost among these are the corpuscular elements of the connective tissue, which is converted into adipose tissue in this manner. The subcutaneous and subserous connective tissue stands first in this respect; next comes the interstitial connective tissue of muscles, and of those especially which are seldom thrown into contraction, or are maintained in a state of rest by disease (ankylosis of joints, paralysis); and lastly, the subfascial, subsynovial, and submucous connective tissues.

§ 63. All these predisposing causes come into operation whenever the blood contains more than its usual proportion of finely-divided fatty matter—whenever there is a *fatty dyscrasia.* We recognise the presence of this condition by a cloudy, opalescent, whitish state of the serum. Under the microscope we may detect oily particles of considerable size; or our examination may yield negative results even with very high powers, if the emulsion is exceedingly fine. Such serum can always be cleared by shaking it with ether. If it is allowed to stand, the oily matter collects on the top, forming a creamy layer.

This *serum lacteum* may always be found about three hours after a meal; and it is not to be wondered at that persons who eat much rich food should get fatty matter infiltrated into their connective tissue (obesity, polysarcia). Further, we know from experience that fatty matters accumulate in the blood of drunkards and persons suffering from pulmonary disease, in whom the fat which is taken into the alimentary canal, and absorbed by the blood, is not completely burned off. In either case the liver is the chief reservoir of the superfluous fat. We also meet with FATTY METASTASES, diseases in which fat is absorbed from one place to be deposited in another. Tubercular diseases of the lungs are not infrequently associated with such metastases from the *panniculus adiposus* to the liver. Since, however, in such cases we may also assume defective oxidation as a cause, those instances are of greater weight in which metastasis of fatty matter constitutes the essence of the disease, or is associated with disease of some organ other than the lung. I once met with a phenomenon of this kind in a woman 27 years old, the fat having been transferred from one place to another in the course of a single fortnight.

II.—ON MORBID GROWTH*

(INCLUDING INFLAMMATION).

1. General Considerations.

§ 64. In natural contrast to those tissue-changes which we have been hitherto considering stands morbid growth. By this term we understand every over-production of tissue-elements. The varieties of morbid growth differ extremely in their relative importance, whether as regards the organ in which they occur, or in their relation to the body as a whole. We were able to assure ourselves that a certain impairment of potential function was constantly associated with every sort of retrograde metamorphosis: this cannot be asserted of morbid growth. We must, however, guard ourselves jealously against inferring any general increase of functional capacity, such as might be expected *a priori* from the contrast between the two orders of phenomena; at most we can only speak of a deviation from the normal standard of functional power; and that is not saying much. To get a sound basis for a comprehensive knowledge of morbid growth, it is both practically advantageous, and quite in accordance with the principles of modern pathology, that we should endeavour, in the first place, to reduce its manifestations to *an excess of physiological growth*, *i.e.* of the normal development and growth of organs. A historic retrospect (which need be very brief) shows us that this principle was always in the mind of our forerunners; but it has never been carried out to its strict logical consequences till now.

§ 65. I will not go farther back than to *John Hunter*. In his celebrated treatise "On the Blood, Inflammation, and Gunshot

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* "Morbid Growth" is here employed as synonymous with "pathologische Neubildung;" the expression is unsatisfactory, but it has the merit of being more English than "pathological new-formation," a barbarism not unfrequently met with.—Tr.

Wounds,"* he developed the idea that an effusion of lymph was the necessary starting-point of all new growth. The plastic quality was regarded by him as a force inherent in the effused material, prompting it to the production of every sort of tissue from its own substance. An independent vascular apparatus is always the first thing to be developed; this is responsible for every farther step in the process; it furnishes fresh supplies of plastic lymph, and so on. Through conceptions of this order—which rested, by the way, on a basis of the most careful observation—we detect a glimmering conviction that the growth is something foreign to the organism, something introduced into it from without—a parasite, to use an extreme term. *Hunter* was led to this conclusion chiefly by comparing morbid growth with the development of the chick in the egg. He knew nothing of the cell, and regarded the *punctum saliens* as the starting-point of all development.

The discovery of the cell, speedily followed by the recognition of cells in the embryo before the existence of a heart, necessarily exerted a modifying influence upon *Hunter's* theory. The development of the vascular system fell back at once into a secondary place; and when it became certain that, apart from the first mapping out of the circulatory system, every development of new vessels was only an extension of the already existing system of canals, the theory of an "independent vascularity" of new growths fell to the ground, carrying with it in its fall a good part of their personal individuality. The question was shifted from "How do new growths originate?" to "What is the origin of cells?" The alternative which had presented itself in the case of the vessels recurred in the question as newly formulated. Theories were at once constructed, based on the *spontaneous generation* of the cell. Plastic lymph, or rather the "plastic quality" of lymph, continued as before to be regarded as the formative cause in the genesis of tissues. It now received the name of cytoblastema, or more briefly *blastema.*

A full discussion of one or other of these theories would lead me too far. Suffice it therefore to say, that the doctrine was at first applied very unconditionally. Blastema, wherever found, was supposed to consist of an exudation of the *plasma sanguinis.*

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* Translated into German by *Hebenstreit* in 1797. Published by Hunter in 1793. Palmer's edition, vol. iii.

In this pure fluid minute granules were first of all developed; these united to form nucleoli, then nuclei, and last of all cells. As time wore on, men grew more cautious; the possibility of cell-formation was made conditional on the presence of at least the elementary granules pre-formed in the blastema.

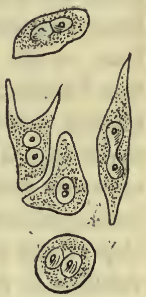
It cannot be denied that a transition period of mixed theories intervened between the original doctrine and that finally established by *Virchow: omnis cellula e cellulâ.* Wherever cells are present in the organism they are the progeny of other cells which have ceased to exist; they inherit the existence, though not always the peculiarities and vital properties, of their progenitors. The question as to the mode in which cells originate was thus permanently settled. The cells which we find among the products of morbid growth likewise owe their origin to the division of pre-existing cells. But of what pre-existing cells? This still demands an answer. *Virchow*, whose authority on this subject has been absolute during a period of ten years, elaborated the theory that the cells situated at the point occupied by the growth undergo multiplication by fission, that the new tissues were actually substituted for a certain proportion of the normal constituents of the body. On the other hand, *Cohnheim* has established beyond all doubt that a migration of colourless corpuscles from the vessels—a plastic exudation in the strictest sense of the word—may supply the materials for morbid growth. Of course, these corpuscles also result from the proliferation of pre-existing cells; but the parent-cells are at a distance from the seat of disease; they are in the blood, the spleen, the lymphatic glands. This, indeed, does not exclude the possibility of growth taking place *in loco morbi;* on the contrary, *Stricker's* recent researches on inflammation afford conclusive evidence that migration is followed by fission of the emigrant cells, and, within certain limits, of those cells also which exist pre-formed at the seat of mischief.

§ 66. Led away by these inquiries into the fundamental nature of the process, observers have in the meantime neglected to institute a more careful comparison of morbid with normal growth. I will endeavour, to the best of my ability, to remedy this defect; but some preliminaries of a general kind must first be settled. And, in the first place, we must not rest content with the bare assertion that cells originate from cells, without being at the pains of acquiring a fuller knowledge of the minuter details of the process. The cells of the adult organism differ very widely and in various ways from the form originally common to all—that of a nucleated lump of protoplasm; the changes which have resulted in their differentiation being connected with their functional activity. Hence we find that in nearly every tissue our series of productive metamorphoses sets out from a different point. We cannot shut our eyes, however, to the constant recurrence of certain common features, by combining which we may very well construct a general plan of cell-production *de novo.*

AN INCREASE IN THE NUMBER OF NUCLEI is never absent in any case of cell-development. It is in the highest degree probable that this increase is due in every case to fission of the original solitary nucleus. Over and over again has this fission of the nucleus been observed. We possess a countless number of careful descriptions, telling us how the nucleus becomes lengthened, how it is narrowed at its middle, exhibiting an hourglass constriction or inflexion, until at length its halves separate from one another, and two nuclei take the place of one (fig. 26).

The nucleolus too seems occasionally to take part in the process. Nucleoli with a central constriction, hourglass-shaped, and double, have been repeatedly observed in the large, vesicular nuclei of cancer-cells, in which the behaviour of the nucleolus admits of being clearly traced. It must nevertheless be admitted that the actual occurrence of fission has been comparatively seldom *seen.* This is easily accounted for by the extraordinary quickness with which the fission takes place. According to all observers who have been lucky enough to see the phenomenon actually take place before their eyes in recent living cells, it is the work of a few seconds. Add to this that it may begin repeatedly, only to recede again; in which case the inflexion which has been formed is again effaced, until, after several abortive attempts, fission is completed suddenly, as though it were a task for the due execution of which repeated efforts were needed. The same remarks apply to the subsequent fission of the cell itself; in either case we must bear in mind the saying of an illustrious naturalist, to the effect that one positive observation carries more weight than any number of negative ones.

FIG. 26.



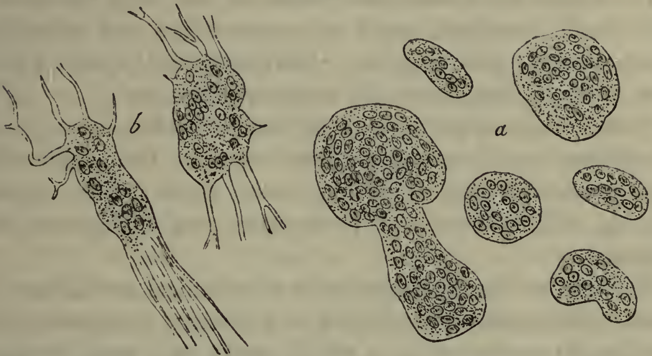
Cells showing fission of nuclei. From a carcinoma.

§ 67. Another phenomenon, which usually accompanies fission of the nucleus, is an increase in the amount of protoplasm. Apart from the *a priori* difficulty of conceiving how, without a proportionate increase in the bulk of the individual cell, it can furnish an amount of matter nearly twice as great as itself, we have the direct evidence of the microscope; this increase in volume having been observed so often that its occurrence is no longer open to any doubt.

Fission of the nucleus, together with increase in the amount of protoplasm, thus make up the first stage in the genesis of cells. The process may be arrested at this point; it may be limited to a repeated multiplication of nuclei with increase in the amount of protoplasm. It then gives rise to those peculiar structures which have been described by *Robin* under the name of *myéloplaques*, or *cellules à noyaux multiples.* These are comparatively large, single-contoured flakes of a very finely granular, feebly refracting material; each flake exhibiting in its interior a large number (as many as twenty to thirty) of round nuclei, furnished with nucleoli. These structures vary greatly in their external form, which is obviously quite independent of any law of symmetry, being determined by the shape of the cavity which they contribute to fill. It is only when these giant-cells (*Virchow*) are found embedded in some very soft and yielding tissue that they assume more or less of a globular, or, at all events, rounded shape (fig. 27 *a*); in tissues with a fibrous structure, the giant-cells are furnished with processes, which must be regarded as prolongations of the plasmatic effusion to which the increase in size of the cells is due, into the interfibrillar interstices. This relation is most instructively elucidated by a case of *Billroth's*, where the giant-cells originated, in the manner just described, from the cellular elements of muscular fibre. At the periphery of the tumour (which was caused, at least in part, by this very phenomenon) *Billroth* succeeded in demonstrating that the muscular fibres were swollen, and their fibrillæ dissociated from one another. The individual giant-cells exhibited the forms figured in fig. 27 *b*. I made a similar observation in the case of a connective-tissue growth in the white substance of the brain. The great point to be borne in mind is, that every giant-cell has really sprung from a pre-existing cellular element; an example of the almost unbounded formative power at the disposal of the organism in the person of each of its constituent cells.

§ 68. The second stage in cell-development is FISSION OF THE CELL itself. Each of the newly-formed nuclei operates as a centre of attraction for the protoplasm which immediately surrounds it; and when this attraction goes so far as to isolate a segment of protoplasm round each nucleus, we say that the cell has undergone division.

FIG. 27.



Giant-cells. *a.* Rounded (*Virchow*); *b.* With processes: from a muscular tumour (*Billroth*).

The microscopic appearances presented by this "segmentation" of the protoplasm are not alike in all cases. The leading differences are due to the degree of cohesion to which the peripheric layer of the parent-cell has attained. This outermost layer is in most cells of extreme tenuity—a "physical membrane," such as is always formed at the junction of two dissimilar fluids which refuse to mingle with each other. The greater the size and the age of the cells, the more distinctly are they seen to be invested by a colourless, homogeneous, highly refractive, double-contoured membrane—a cell-membrane in the old sense of the word.*

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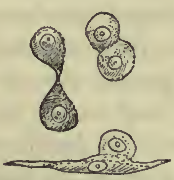
* *M. Traube* tries to find a chemical explanation of the phenomenon in the precipitation of an albuminous constituent of the protoplasm by another colloid (*Graham*) substance acting upon the cell from without. *Kühne's* experiments on Infusoria (Amœbœ) agree very imperfectly with this hypothesis. It is very certain that a membrane appears on the surface of the amœba in consequence of *external irritation;* but *Kühne* finds that the membrane-producing irritants are rather of a physical than a chemical nature (electricity, alterations in temperature); hence *Kühne* contents himself with defining the membrane-formation simply as a peripheral coagulation of the protoplasm.

The physiological cell-growth which accompanies or causes the growth of the entire organism, seems to be confined to such cells only as are either destitute of a limitary membrane, or furnished with a mere "physical investment" of extreme delicacy. Under these conditions fission of the cells, like that of their nuclei, manifests itself as a constriction and subsequent division of their body (fig. 28). The longitudinal splitting of the fibres of striped muscle is only a variety of fission.

To this mode of cell-division by fission, morbid histology adds two further types, or, to speak more correctly, two modifications in the anatomical features of the process. These are, the development of cells in nucleated protoplasm, and endogenous cell-formation.

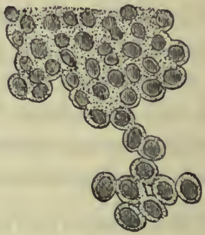
The first of these presupposes two anatomical conditions; the parent-cells must be quite devoid of a limitary membrane, and a considerable number of such wholly naked cells must be aggregated together. Under these circumstances the protoplasm of any cell will *seem* to be uninterruptedly continuous with that of neighbouring cells; the outlines of separate cells are not distinguishable; and this of course applies equally to the outlines of the newly-formed cells. Should such cells divide, our only way of detecting their division would be by noticing that two nuclei, resulting from the fission of a single one, and originally in close contact, have moved away from one another to a slight extent. We cannot actually *see* more than the various stages in the division of the nuclei.

FIG. 28.



Cells undergoing fission. *a.* From a luxuriant granulation; *b.* Division of fibre of striped muscle.

FIG. 29.



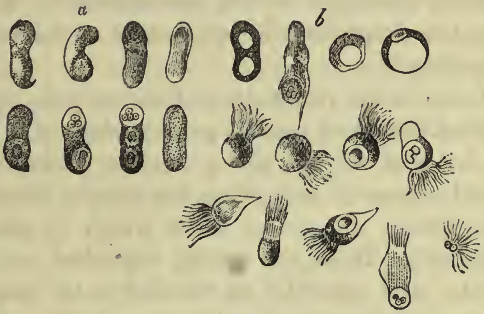
Nucleated protoplasm: fragment of a granulation.

We find this nucleated protoplasm in the most luxuriant forms of cell-proliferation, such as granulations, soft cancer, and sarcomata. It differs from the multinuclear giant-cells by its greater bulk on the one hand, by its behaviour towards reagents on the other. For while the giant-cells maintain their continuity under all circumstances, the addition of a small quantity of acetic or chromic acid suffices to separate the nucleated protoplasm into its component cells. In these cases we may often see a shred of the nucleated tissue bounded by an arcuate or crenated border of a darker hue, where it is in contact with the acidulated fluid; each individual arc corresponding to an isolated segment of the circumference of one of the constituent elements of the protoplasmic mass (fig. 29).

Endogenous cell-formation must also be regarded as a modified variety of fission. Should a cell with a well-defined limitary membrane, such *e.g.* as an oldish epithelium or cancer-cell, be stimulated to production, the process confines itself to its inner, semi-fluid portion.

It is here that the nucleus divides, and the protoplasm groups itself round the newly-formed nuclei. The resistance of the cell-membrane prevents the independent segments from separating; and thus we obtain a more or less characteristic example of a *parent-cell containing a brood of daughter-cells* (fig. 30 *a*). It is self-evident that the daughter-cells are smaller in size than the parent-cells; they are always round, and usually resemble pus corpuscles. It by no means follows that every one of the nuclei resulting from fission of the original nucleus should become the centre of a daughter-cell; on the contrary, one or more nuclei

FIG. 30.



Endogenous cell-formation. *a*. Development of pus-corpuscles in epithelial cells; *b*. Brood-capsules.

remain over, giving colour to the theory that the whole process of endogenous cell-formation is independent of the nucleus, and consists of a spheroidal segmentation of the protoplasm, together with a *generatio æquivoca* of the nuclei. This question, for the present at least, must remain an open one.

We are possessed of details, which are upon the whole very accurate, concerning the mode in which these endogenous cells are set free. The unsegmented portion of the parent-cell may be dissolved in the surrounding fluid, the included cells becoming *eo ipso* free; or the included cell may slip out of its parent. In the latter event a small quantity of fluid usually gathers round the daughter-cell, thus loosening it from its bed; it then slips out by aid of its own amœboid contractility. After its escape the cavity in the interior of the parent-cell ceases to enlarge. The appearance which is left has been compared by *Virchow* to a circular hole punched out of the parent-cell (fig. 30 *b*). The old designation of these structures as brood-cavities or brood-capsules (Bruträume oder Brutraumzellen) may be retained, though *Virchow*, in discovering them and giving them a name, started from the mistaken notion that the empty cavities were primarily developed in the parent-cells by a process of vacuolation, the daughter-cells originating in the vacuoles by a *generatio æquivoca.**

§ 69. It lies in the very nature of the subject, not only that the histological details of morbid growth admit of a generalised exposition, but that we can also give some preliminary notions of a general character respecting the coarser features of the process, respecting the *forms* under which it presents itself to the naked eye. These are mainly dependent on the locality of the growth, and especially on whether it be situated in the parenchyma of an organ, or more towards its surface. I am well aware that no distinction of this kind can be strictly and universally applied; but then we are concerned not so much with the logical perfection as with the practical utility of our definitions. We have to define technical terms devised by the physician to meet his daily wants. We are not trying to classify the products of morbid growth, but to give the reader a general view of their coarse morphology.

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* *Volkmann* and *Steudener* suggest that the intussusception of one cell by the soft body of another may simulate the aspect of endogenous cell-formation. To a certain extent this is undoubtedly true, particularly in the case of epithelioid cancer-cells; but I cannot think that the whole doctrine of endogenous cell-formation should be brought in question on account of the possible chances of an error of observation—an error too which it is not difficult to guard against.

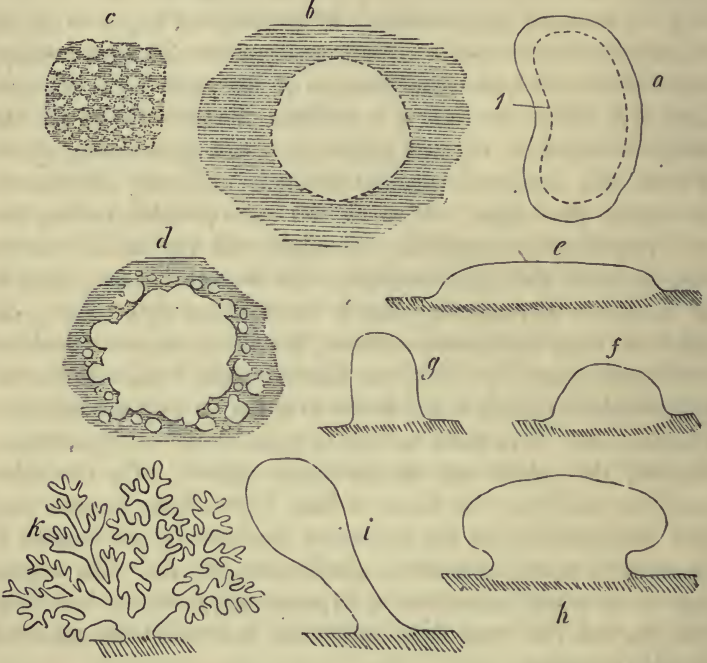
A. When the products of morbid growth are situated in the parenchyma of organs, they may present themselves as—

1. A UNIFORM ENLARGEMENT of the affected organ in all its dimensions (*intumescentia*). This is synonymous with hypertrophy, in the oldest and least scientific sense of the word. The enlargement may either be due to a uniform overgrowth of all the tissues of which the organ is made up, or to a quantitative excess of some one structural element which is uniformly distributed throughout the organ. Were it not more prudent to drop the word hypertrophy altogether, we might call the former variety *true*, the latter *false* hypertrophy. The former is exemplified in the muscular hypertrophy due to exercise—a hypertrophy in which not only the muscular fibres, but the perimysium and the vessels take part; so that, on microscopical examination, the hypertrophied muscle is not found to differ in any respect from a normal one. The same is true of some forms of hypertrophy affecting the spleen and the lymphatic glands. On the other hand, we must give the name of false hypertrophy to such uniform enlargements as are due to an increase in the amount of interstitial connective tissue in glands, muscles, &c. The vagueness of our whole conception of hypertrophy, however, is obvious from the fact that even fatty infiltration is occasionally admitted into this category.

2. A KNOT (*nodus*). By this we understand a circumscribed tumour more or less globular in form. In size it may vary from a granule barely appreciable to the naked eye to that of a man's head. Its size is solely and directly proportional to the amount of newly-formed tissue. On cutting through an organ in which a mass of this sort is embedded, we find it protruding more or less above the surface of section. Hence we may justly infer that it must exert some measure of tearing, stretching, and dissociating force upon the healthy parenchyma which surrounds it. Hence too its tendency to grow in the direction of least resistance, so that when it happens to be situated at or near the surface it causes a globular protuberance. The degree in which

all these properties are manifested varies directly as the amount of newly-formed tissue, inversely as the amount of tissue replaced by the morbid products. The less the quantity of parenchyma which has been used up, the more does the growth tend to squeeze it and to protrude from it. There are knots which, as soon as they have arrived at a certain, and that by no means striking size, cease to grow by extension of the morbid action to the contiguous parenchyma (growth by apposition), and proceed to increase by proliferation at their centre (central growth). The knot then acts almost as a foreign body. The mechanical irritation of surrounding parts, alluded to above, assumes so

FIG. 31.



Naked-eye forms assumed by products of morbid growth: diagrammatic. The shaded part denotes the normal parenchyma. *a.* Uniform swelling of a whole organ; *a* 1. Its normal outline; *b.* The knot (*nodus*); *c.* Infiltration; *d.* Growth of a knot by infiltration; *e.* Flat intumescence; *f. Tuber; g. Papilla; h. Fungus; i. Polypus; k.* Dendritic outgrowth *(papilloma).*

great an intensity as to lead to chronic inflammation, and the production of connective tissue. As the size of the knot increases, the connective tissue presents more and more the appearance of a capsule, continuous with the knot only at scattered points of its surface—those, namely, where the vessels enter it and leave it; elsewhere it is smooth and humid, often lined with pavement-epithelium. The continuity of the capsule with the knot must originally have been universal. The partial solution of this continuity demands explanation, and this explanation can only be of an indirect kind.

I presume that all observers are agreed in regarding the interstitial cavities of the connective tissue (*e.g.* the bursæ mucosæ), as produced by the movement of organs as a whole upon one another, the space required for this play being furnished by a partial softening of the connective substance. The wide meshes of the areolar tissue are the simplest, the articular cavities the most complex, examples of this arrangement. The case with which we are now concerned is in all respects analogous to the movement of one of the internal organs upon another, inasmuch as no increase in the superficial area of the knot can be imagined to take place without some displacement of its points of contact with neighbouring parts. Embrace the right fist with the palm and fingers of the left hand. On gradually extending the fingers of the former we get an approximate illustration of the phenomenon in question. The doctrines held on this subject by the generation immediately before our own, differ from those now adopted, just as the old view of brood-capsules differs from ours. The capsule was considered as a pre-formed cystic or cellular cavity, into which the "neoplasm" was subsequently poured.*

3. AN INFILTRATION. This term occurs here for the second time, though used in a very different and very inappropriate sense. When we speak of a tubercular infiltration of the lungs, of a cancerous infiltration of the liver, we mean a uniform swelling and condensation of large portions of these organs,

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* Hence the old division of tumours into cystic and non-cystic. The former division coincided with benign, the latter with malignant, growths. We shall hereafter see what measure of truth was here attained by the practical instinct of the physician.

due to a deposition of the morbid products in a very large number of minute foci. Infiltration is thus intermediate between uniform intumescence on the one hand, and nodal growths on the other. It need hardly be added that they pass into each other by countless gradations. Should, *e.g.*, the tubercular foci be somewhat larger and more isolated than usual, the infiltration becomes a collection of granulations. When we find a circumscribed and solitary deposit of tubercle, as we sometimes do in the brain, we call it a tuberculous nodule. So too, we commonly find a zone of infiltration round such knots as increase rather by peripheral apposition than by central growth. In these cases we may see, even with a simple lens, the creeping extension to neighbouring parts, in which continuity with the parent knot is never interrupted, associated with a *per saltum* advance, fresh nodules being developed independently at short distances from the periphery of the primary centre; these enlarge, and finally coalesce with the central knot. Such a zone of nodules may justly be termed a zone of infiltration. Hence the phrase which continually recurs in post-mortem records—"the parts adjoining the tumour were already infiltrated." The transition from infiltration to uniform intumescence is determined by the degree of extension of the infiltrated parts. Should the entire organ be infiltrated, it is hard to see why we should not call it uniformly swollen.

B. When the morbid products are situated on the surface of an organ they assume the form of—

4. A DESQUAMATION (*desquamatio*). This term is restricted to an abundant shedding of epithelial cells. Should it be attended by a considerable secretion of fluid, we call it a catarrh; thus generalising a term primarily applied to catarrh of the mucous lining of the nasal fossæ, in the course of which the morbid secretions flow down from the nasal cavities (*καταῤῥεῖ*).

5. A FLAT, TABULAR SWELLING (beetartige Anschwellung). This corresponds to the "uniform enlargement" of parenchymatous organs, like which, also, it is occasionally called "hypertrophy." Here too, the distinction between true and false hypertrophy recurs. It differs from true hypertrophy in never involving the whole of a cutaneous or mucous surface; it may extend over large tracts of it, but is always separated from the healthy structure at some point or other by a distinct line of

demarcation; to this peculiarity it owes its occasional name of "insular intumescence." It occurs in the course of many chronic inflammations of the skin and of the arterial coats, in enteric fever, and in many forms of cancer.

6. A TUBER. The area occupied by the base of any circumscribed swelling remaining constant, its progressive increase in height makes it more and more of a tuber. The outline and height of a tuber may vary within certain limits; when much elongated it is termed a wart (*papilla*). The base of a tuber, however, always remains its broadest part. Should its base be narrowed its edges necessarily come to overhang it, and the growth becomes—

7. A FUNGUS; or,

8. A PEDUNCULATED TUMOUR (*polypus*). The distinction between a fungus and a polypus depends essentially on the mode in which the constriction at the base of the tuber is brought about. Should this be merely relative, *i.e.* due to excessive proliferation in the distal portion of the tuber, we call the growth a fungus. The fungus has a broad pedicle and a flattened top. Should this relative narrowing of the base be associated with an absolute contraction, by the dragging of the head as its size increases, whether by its own weight or the application of external force, the base gets narrowed down to a relatively thin stalk, and a polypus is the result.

9. A CAULIFLOWER GROWTH. This is undoubtedly the most complex form which can be evolved from a circumscribed elevation of the surface. As its name implies, it is constructed on a dendritic type. We have a trunk which gives off branches at different angles; on the smallest twigs we occasionally have leaves or berries. Glands with branching ducts are similarly constructed (those known as acinous glands). The analogy between the first mapping out and early development of these glands and that of the dendritic vegetations from cutaneous and mucous surfaces is very striking. We shall return to it more at length when we come to speak of these growths in detail. Suffice it for the present to say that in the dendritic outgrowths, as in the acinous glands, the essential part of the entire formation is to be sought in the ultimate elements of their structure. And here the ultimate element is the elongated tuber—the papilla. And indeed no other view harmonises so well with the

known course of development in dendritic outgrowths. A simple papilla is in every case the starting-point of the whole series of changes; at some point of its surface it gives off a lateral sprout, a fresh papilla; we thus get a forked process, or a trunk with two branches. The phenomenon repeats itself, and underlies the most complex ramifications of the morbid growth.

In bringing this general view of the subject to a conclusion, I would remark that the morphological nomenclature given above is very lax—that the terms pass into one another by imperceptible gradations; and I insist on this fact mainly because it gives me another opportunity of combating the pre-histological delusion that, when we have described the naked-eye appearances of a new growth, we have got any nearer to its essential characters. This mistaken notion was excusable enough so long as minute investigation had to contend with greater difficulties than those which now beset its path; it was excusable, moreover, because certain morbid growths adopt one form in preference to others; nay, some of them occur *only* as fungi, as polypi, as papillæ, &c. But this, of course, does not preclude other products of morbid growth from assuming the same forms. And what is true of external form is equally true of the remaining naked-eye characters—of size, consistency, and colour—all of which have been employed as principles of classification in the same mistaken way.*

§ 70. By way of appendix, I will here allude to a peculiar element of structure which may complicate the most various forms of morbid growth—I mean the CYST. This term includes every sharply circumscribed globular or spheroidal cavity filled with fluid. This definition does not take the cyst-wall into account; for although a special cyst-wall, or sac (Balg) is often present, yet it is not invariably so. The contents of different cysts differ widely from one another. They may be thin, and clear as water; they may be greasy or pasty; nay, they may even be so thick as hardly to allow of their being called fluid at all. These varieties essentially depend upon the mode in which the cysts originate. And here we have to discriminate between—

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* Particularly as regards tumours. Cf. *Virchow*, "Die Lehre von den Krankhaften Geschwülsten." Berlin. 1864.

a. *Retention-cysts.*—These cysts originate, as their name implies, in the retention of secretions: we may add that the secretions are invariably such as would naturally be voided on the free surface of the body, whether skin or mucous membrane, and then removed or otherwise disposed of. The presence of a recess or diverticulum, of a cavity open at one end and closed at the other, is necessary for the production of a retention-cyst. This cavity is shut off by some accident, and converted into a cyst by the retention of the matters which continue to be uninterruptedly secreted, and which therefore accumulate at their place of origin. Such conditions are obviously most common in the physiological recesses of the skin and mucous membranes, in the ducts and terminal cæca of the tubular and acinous glands; that similar conditions may also occur elsewhere will be shown farther on.

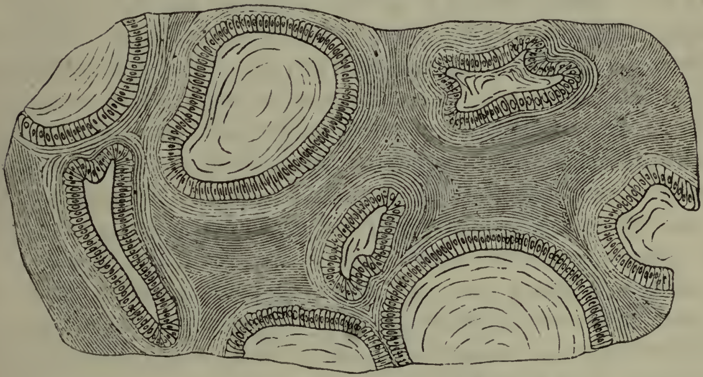
On inquiring into the causes which may lead to closure of the efferent duct of a gland, we are met by various possibilities. The simplest, yet least common mode, is that by plugging of the duct (*obturatio*). Solid bodies, whose size and weight do not allow them to pass through the ducts, nearly always originate as precipitates, or concretions from the fluid secretion itself, *e.g.* biliary, urinary, and salivary calculi. More rarely the efferent ducts of a gland are stopped up by solid matters of extraneous origin, *e.g.* hydatid vesicles. Again, a duct may be obstructed by mutual adhesion of its walls (*obliteratio*). Causes which predispose to this mode of obstruction are external pressure, and a raw, ulcerated condition of the surface, particularly when this is followed by cicatrisation. When incomplete in degree it is known as stricture (*stenosis*, *strictura*). Finally, pressure from without (*compressio*) is sufficient of itself to narrow, pucker, and constrict the duct. This last mode of closure, which usually becomes complicated at a later period with "obliteration," is of prime importance as regards new growths; for not only are such growths in the neighbourhood of the urinary passages, the pancreatic and choledoch ducts, capable of closing these great efferent canals by compression and constriction, giving rise thereby to colossal dilatation of that part of the mucous tube which is above the point of obstruction, but the same process is repeated on a small scale whenever a new growth involves the gland-substance itself. Single uriniferous tubes, lacteal ducts, tubuli seminiferi, &c., are constricted by interstitial morbid growths; the secretions accumulate: the longer this lasts the more does the original form of the isolated cavity (*sc.* that of a hollow cylinder) give place to a spherical or spheroidal shape; a cyst is formed, whose walls are identical with those of the original duct, whose contents are (at least in the earlier stages of the process) identical with the proper secretion of the gland.

A rare, but on that account all the more interesting variety of retention-cysts, is that which originates, not in the ducts of glands, but in the interstitial and intercommunicating lacunæ which are left between the trunk, branches, and terminal papillæ of dendritic vegetations. It does not appear, at first sight, as though these interstitial lacunæ were in anywise fitted for conversion into cysts. Not only do they freely communicate with one another, but they are everywhere in such free communication with the external medium, that it would be an abuse of language to speak of orifices, or of a plugging of such orifices. This is true, and continues true, so long as a dendritic growth is situated upon a free and level surface. But matters take a different turn when the growth starts from the inner surface of a cavity. Take a papilloma protruding from the external os into the vagina. A time must needs come when the growth fills the canal of the vagina so completely that its walls begin to exert a lateral reaction upon the tumour; and this counter-pressure must increase in proportion to the bulk of the tumour. The papillæ are bent towards each other; their convex surfaces are made to touch; they ultimately coalesce along the lines of contact, and thus convert the open inter-papillary space into a number of minute, tubular crypts which differ from tubular glands only by appearing, in transverse sections, to be bounded, not by circular outlines, but by three or four arcs, convex inwards, arcs which correspond to the convex surfaces of the contiguous and coalescent papillæ. These tubes are quite as well adapted as gland-tubuli for the development of cysts; all that is required, indeed, for the occasional closure of one or other of these inter-papillary spaces at its external orifice, or at some point in its continuity, being a continued operation of the same external pressure; and so a retention-cyst is formed.

This is an excellent opportunity for realising how any accumulation of fluid tends to transform the cavity in which it is contained, whatever its original shape, into a sphere (fig. 32). Before retention begins the inter-papillary spaces exhibit, on transverse section, triangular and four-cornered figures with incurved sides and very acute angles, figures such as necessarily follow from the apposition of cylindrical bodies. As the fluid accumulates, the acute angles open out. They pass through a parabolic into a simple curve. The inflexed sides, for their part, are gradually depressed till their convexity is quite effaced; and these two sets of movements co-operate to give the space a circular figure when cut across—the cavity becomes globular.

It would lead me too far were I to attempt in this place to give a detailed analysis of the physical law which governs this series of phenomena. I will content myself with reminding the reader that of all stereometric bodies the sphere is that in which the capacity is greatest in proportion to the area of its surface. So long, therefore, as the contents of a body continue to increase in amount, without any corresponding extension of its internal surface, the body must necessarily tend to assume a spherical form. The present is a case in point. I may add that the principle which we have just seen illustrated by a single example is one of very frequent application in the organism. I need only allude to the shape of the eye, of the urinary and gall-bladder, of the heart, &c.

Fig. 32.



Papilloma cysticum from the portio vaginalis, showing conversion of inter-papillary fissures into retention-cysts.

b. *Exudation-cysts.* These, too, are secreting cysts. Their mode of origin, however, is diametrically opposite to that of retention-cysts. The shut sac is not in this, as in the former case, produced by the isolation of a cæcal recess; it is pre-formed. The foundation for exudation-cysts is laid in mucous bursæ, in the sheaths of tendons, in serous sacs, in the ventricles of the brain and cord. Moreover, the accumulation of fluid is due, not to the continuance of the normal secretion, but to an exudation of serum from the blood, transcending the normal standard, and containing salts, albumen, fibrinogen, and extractive matters in the most variable proportions. Exudation-cysts have but little to do with morbid growth. We shall come across them again under the most diverse names—most of which are derived from the watery nature of their contents—as dropsies, hygromata, hydatids, &c., of the different organs of the body. Of greater moment for our present subject are the—

c. *Extravasation-cysts.* A parenchymatous hæmorrhage may readily serve as the starting-point for the development of a cyst. It were difficult indeed to give the name of a cyst to a shapeless clot of extravasated blood not smoothly and sharply marked off from the neighbouring parenchyma, but leaving it irregularly torn and broken up. The extravasation may in some cases, however, present the characters of a cyst from the very first, *sc.* when the blood has been poured out between two surfaces which are naturally smooth (*e.g.* between periosteum and bone, between cartilage and perichondrium), and continues in a fluid state; or it may be converted into a cyst by the production of a layer of connective tissue from the adjoining parenchyma on the one hand, while on the other the blood itself undergoes a series of metamorphoses, ending in its being almost wholly absorbed and replaced by a clear fluid.

d. *Cysts due to softening.* In studying the various "conditions of involution" to which the tissues are liable, we came across more than one process which led to softening—to the formation of a morbid fluid. I allude more particularly to fatty degeneration and mucous softening, the former of which, under certain conditions, may yield a milky emulsion, the latter a fluid clear as water, containing mucus and albumen. Should the escape or the absorption of these fluid products of softening be hindered, their local accumulation, without farther change, may offer all the characters of a cyst due to softening. It will do this more especially when it is shut off by a smooth and sharp boundary-line. That such limitation of a cyst due to softening is not brought about by any membrane capable of being anatomically isolated, lies in the very nature of the thing. The presence of such a membrane may very well be simulated, however, by all the textural elements situated on the confines of the affected region being in the same stage of metamorphosis, and thus forming a layer which differs equally from the healthy parenchyma and from the fluid products of softening.

So long as one of these cysts continues to enlarge by the extension of softening to surrounding parts—so long, in a word, as it remains a mere "centre of softening" (Erweichungsheerd), it has no true limitary membrane. But a cyst originally due to softening may subsequently obtain a lining membrane. In a case of this sort, the softening process comes to a standstill, and the adjacent tissues are organically marked off from the softened part. Like all interstitial cavities in the parenchyma of the body (whether physiological or morbid), the cyst is lined by a continuous layer of connective tissue, which may, under certain conditions, become coated with epithelium. It is then analogous in all respects to a bursa mucosa. Any changes which the contents of the cyst may subsequently undergo depend on their relations with the blood-vessels ramifying in the lining membrane: should they increase in amount, their increase is due to exudation from the blood. The cyst due to softening may thus become a secreting cyst.

In conclusion, let me repeat what I have said already in the course of the foregoing pages, that for the history of morbid growths retention-cysts are of prime importance; next come the cysts due to softening and the hæmorrhagic cysts; while the exudation-cysts have next to no connexion with the subject. In the nomenclature of morbid growths we usually employ the prefix *cysto*, to denote that they are complicated with cysts; thus we speak of cystosarcoma, cystocarcinoma, &c.

2. On Normal as a Type of Morbid Growth.

§ 71. The preliminary observations of a general character contained in the foregoing sections have brought us to a point at which it becomes necessary to classify the products of morbid growth. Now their minute structure affords no adequate basis for classification; we must seek aid from some principle of a broader kind, and such a principle can only be found by attempting, as already suggested, to institute a careful comparison between the phenomena of morbid and those of normal growth. We must distinguish between the initial and the later stages of normal growth, for it is chiefly among the latter that we find the analogies of which we stand in need.

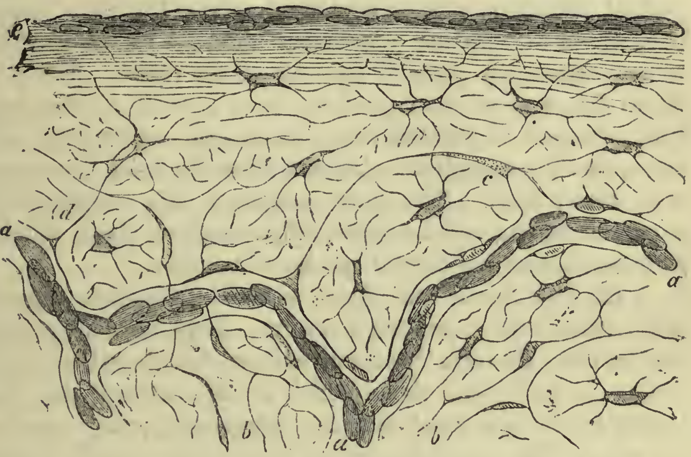
The first foundations of every organ are laid by the differentiation of elementary parts which are originally equivalent. These elementary parts are small round cells, furnished with large nuclei; the blastoderm and *area germinativa* are formed by a continuous aggregation of these cells. The separation of the blastodermic membrane into three layers, which next ensues, has recently been subjected to much discussion. So much appears certain, that the organs of locomotion and sensation are developed from the upper layer; from the under one those of respiration and digestion, while the middle layer is destined to form the blood-vessels and the connective tissues. *His* believes, however (and his view is to some extent confirmed by *Waldeyer's* researches), that from the very first moment of this subdivision there exists an absolute contrast or opposition between the upper and lower (two outermost) strata of the blastoderm on the one hand (the organopoietic strata proper, which, taken together, form the *neuroblast*), and the intermediate layer, the *hæmoblast*, on the other; the latter being formed, not, as has hitherto been supposed, by a splitting of the inferior layer of the blastoderm, but by an independent ingrowth from the edges of the *discus proligerus*. It would indeed be interesting to find the independent character of the blood-vessels and the parenchyma, of the *nutriens* and the *nutriendum*, shadowed forth even in these earliest stages of development. The mutual independence of these two great components of the organism is definitively established, when the first rudiment of a vascular apparatus, the *area vasculosa*, makes its appearance; and there can be no doubt that it affects the ulterior development of the individual most profoundly. From this time forth, no sooner is any new organ differentiated from the continuous aggregate of embryonic cells, no sooner do we gather from the mode of aggregation of the specific elements that a muscle, a nerve, a gland, &c., is being formed, than the vascular system sends a looped process into it, and takes possession of the new territory, as it were, in the name of the organism as a whole. Every fresh vascular loop is an outgrowth from a pre-existing loop, so that the unity and independence of the entire system remain preserved. This law continues in force throughout the whole course of subsequent growth, and is manifested afresh in the adult organism whenever the occurrence of morbid growth gives it an opportunity.

Passing now to the consideration of these later stages in the growth of organs, we are unhappily obliged to admit at starting that our knowledge concerning them is still very defective. It is only about the growth of bone that we possess adequate data. The mode of growth of epithelium is a question which presses for a solution. A few scattered facts are on record concerning the growth of the muscles and tendons. The main point, the central fact, which requires to be established in all these cases, is the relative share in the formative processes taken by the specific and functionally active elements of each organ on the one hand, by the conjoint vascular and connective-tissue system on the other; the latter system, in its entirety, will henceforth be termed the internal or intermediate apparatus of nutrition.

A description of the growth of THE INTERMEDIATE APPARATUS OF NUTRITION itself forms the best introduction to a brief review of these processes. As regards the most important of its constituent elements, the VESSELS, we follow *Billroth* in discriminating between three modes of vascularisation *de novo* (Gefässneubildung). The *primary mode*, which occurs only in the *area vasculosa*, consists in a direct differentiation of the embryonal cells into red blood-corpuscles on the one hand, and the structural elements of the vascular walls on the other. We can see the cells closing up along certain definite lines, to form denser cords; those axially placed next assume a red colour, and begin to move in a clear fluid which collects round them; while those at the periphery, remaining stationary, *eo ipso* represent the vascular walls. The walls of the new vessel are not indeed marked off from the surrounding parenchyma by any distinct boundary-line; on the contrary, we get the impression of a continuous mass, through which canals are tunnelled in every direction; moreover, single cells continue here and there to separate from the islets of parenchyma, and to enter the blood-current, where they are converted into blood-corpuscles. Such phenomena as these, however, are only apparently contradictory to the well-known structure of the apparatus when complete. The very next step clears up this point. This step is the formation of an endothelial lining to the vessels, which is justly regarded by *Eberth* (*Stricker*, "Manual of Histology," Syd. Soc. transl., i. 264) as the essential basis, the only universal and characteristic element of the vascular wall. With the formation of the endothelial tube, which, as the reader is aware, consists of a very delicate membrane, made up of elongated, polygonal, nucleated cells, all detachment of cells from the inner surface of the vascular wall is at an end, and a definite boundary-line is established, beyond which the parenchyma, in the broad sense of the word, may be said to begin, whether it consist, as in the present case, of embryonic tissue, or of connective substances, or of connective tissue with muscular fibres, &c.

The completion of the endothelial tube brings the process of primary vascularisation to a close. Should a new vascular loop be required, it can only be formed by a protrusion of the endothelial tube. Such a protrusion is therefore constantly associated with those modes of vascularisation which *Billroth* calls secondary and tertiary. It occurs most manifestly in the *tertiary* mode. In this variety cæcal protrusions may readily be seen to occur at certain points in such capillary vessels as are already pervious; these gradually extend, and finally bend round in the form of an arch, to rejoin the parent vessel; or two such protrusions may meet each other, with the like result of producing a new capillary loop by their union. A more minute examination demonstrates the presence of certain fine, threadlike processes, whose exact relations are rather hard to determine, in connexion with these cæcal protrusions (fig. 33). The best object for this investigation is undoubtedly the transparent border of the tail of a tadpole; but even here the vessels are surrounded by a number of stellate connective-tissue corpuscles. Should we find the protrusions from the capillaries continued into these corpuscles, they may be viewed as identical with the threadlike processes, and we infer that the development of the capillaries takes place by a direct metamorphosis of corpuscular elements; should we fail, on the other hand, in demonstrating any such continuity, the threadlike processes will have to be regarded as peculiar structures, which serve to map out the course of the future vessels. Long and patient investigations have led to the conclusion that either alternative is possible. The capillary protrusions neither seek nor avoid the corpuscular elements. The direction of the future vessel is determined by conditions of a more general order; should it happen to coincide with a neighbouring cell, this takes part in forming the wall of the vessel; should it coincide with

FIG. 33.



Tertiary vascularisation. Border of tadpole's tail. *a.* Capillaries; *b.* Lymphatics; *c.* Vascular buds; *d.* Ditto, in connexion with a connective-tissue corpuscle; *e.* Free border, with epidermis.

the boundary-line between two adjacent cell-territories, we see the vascular bud taking an independent course. According to *Stricker*, the outer surface of the capillaries is continuously coated with a thin layer of protoplasm; the protoplasm is not confined to the nucleated points; and this view would at once provide us with materials for the development of our vascular buds. That these really consist of protoplasm is shown, on the one hand, by their optical similarity to the protoplasmic processes of the connective-tissue corpuscles; on the other, by the fact that these processes can take their place in the development of new vessels. When the new capillary is thrown open to the blood-current, the protoplasm forms a thin layer over the entire surface of the tube. It then stiffens, forming a membrane which differs in no respect from that of the parent-vessel, with which, indeed, it is uninterruptedly continuous. Should connective-tissue corpuscles have taken part in the construction of the new vessel, they take their place, after the metamorphosis is completed, among the constituent elements of the endothelial tube.

Secondary vascularisation is almost exclusively confined to the domain of pathology; it may be regarded as a modification of the tertiary mode in so far as it also is associated with a gradual dilatation of the endothelial tube. It differs from it, however, in the greater prominence assumed by the apposition of new elementary parts to the wall of the vessel. The course of the future vessel is mapped out by a cord of spindle-shaped cells, arranged in parallel rows; these cells undergoing direct conversion into endothelial elements when the axial *lumen* comes to be thrown open. The many varieties of this secondary mode of vascularisation will be more fully examined under the head of Inflammation and several species of tumours.

§ 72. The second constituent of the intermediate apparatus of nutrition is the CONNECTIVE TISSUE. From the embryological point of view, the term "connective tissue" embraces that residual portion of embryonic tissue which is left between the blood-vessels on the one hand, and the functionally active tissues on the other. The parenchymatous islets of the middle layer of the blastoderm are either used up or pushed aside during the development of the organs; and in proportion as they undergo one or other of these alternatives, we find the organs provided with a larger or smaller amount of connective tissue. In some organs hardly any connective tissue can be shown to exist, as *e.g.* in the kidney and the testicle; the lobules of the liver appear to be exclusively made up of capillary vessels and secreting cells. Yet it is possible to discover with absolute certainty small quantities of unformed connective tissue both in the testicle and in the renal parenchyma; and where even this minimum is lacking, as in the hepatic lobules, the connective tissue is represented by the capillary walls themselves. For the cells of the endothelial tube are equivalent to those of the connective tissue; indeed, we have already seen that the latter are capable of directly replacing the former in the tertiary mode of vascularisation. Moreover, *Ranvier* has found that the cells of the lax subcutaneous connective tissue may exhibit a flattened form; this shows that the connective-tissue corpuscles are generally disposed to adopt the form of thin lamellæ when they happen to lie in interfibrillar spaces of considerable size. The evidence as to the homology of the connective-tissue corpuscles with the cells of the endothelium is completed by the homology of their formative products, products which both are capable of yielding in a certain measure, as we shall see hereafter. Of course I refer only to the stationary cells of the connective tissue, to the connective-tissue corpuscles of *Virchow;* my remarks must not be taken to apply in any sense to the mobile cells discovered by *v. Recklinghausen.*

The connective tissue extends wherever the vessels extend, and even beyond them. It gives an outer coat to the vessels, it serves to continue their walls into the interstices of the organic structures, and inasmuch as all the vessels are interconnected, the vascular system together with the connective tissue constitutes an elaborate framework, in which the remaining morphological elements of the body are embedded. In a word, the connective tissue is so extensively distributed throughout the body, that it is impossible to make a cut at any point without damaging the connective tissue, without exposing it at numberless points of the cut surface.

§ 73. Let us now glance at the conditions regulating its growth. Observers are all but unanimous in holding that for the production of any quantity of connective tissue a proportional quantity of embryonic tissue is required. The latter consists of nucleated particles of naked protoplasm, forming in the aggregate a very soft and elastic substance, of a pale-grey hue. It is very readily generated wherever the need arises for an extension of the intermediate apparatus of nutrition; and it is certain moreover that the required amount of embryonal connective tissue is produced by the intermediate apparatus of nutrition itself. This is one of its most fundamental properties and functions, and unquestionably plays the most important part in morbid growth. It is only the *mode* of its production which is still in urgent need of elucidation. I say "still," inasmuch as the importance of the question for our general conception of morbid processes is so great, that it may justly be regarded as the corner-stone of all past and present systems of pathology. For the embryonal connective tissue, with whose genesis we are now concerned, is identical with the much-discussed embryonic tissue (Keimgewebe) of morbid growth, with the plastic exudation of the humoralists, with *Virchow's* "proliferation of connective-tissue corpuscles," with the accumulation of emigrant leucocytes discovered by *Cohnheim.* When we come to discuss the theory of inflammation we shall have occasion to become acquainted with the data afforded by morbid histology in reference to this question; suffice it for the present to say that the possibility of the migration of colourless blood-corpuscles, and the production of plastic exudations by their accumulation and aggregation, has been placed on a sure footing; while, on the other hand, the farther possibility of fission of the pre-existing stationary corpuscles is not excluded; nay, must in certain cases be considered indispensable.

§ 74. The subsequent metamorphoses of the young connective tissue, the formation of intercellular substances of different kinds, and the resulting constitution of the various members of the connective-tissue series, I must assume the reader to have learned from books on normal histology (see *Rollett's* article in *Stricker's* Handbook, Syd. Soc. transl., vol. i.). We will do well to distinguish rigorously between such connective substances as constitute independent organs, or parts of organs, between the formed or functionally active connective substances (cartilage, bone, tendon, &c.), and the formless, passive connective tissue, which serves only to fill up gaps, and which the older authors called "cellular tissue." Henceforth I shall employ the term "connective tissue" to designate the latter variety only; it is to this variety alone that the statements made above concerning the ubiquity of connective tissue in the human body, concerning the affinity of its cells to those of the endothelium, concerning its significance as a proximate constituent of the intermediate apparatus of nutrition, refer. I must not be understood to question the relationship of this variety of connective tissue to the formed connective substances (geformte Bindesubstanzen); on the contrary, it will appear in the sequel that a clear idea of their relationship is of peculiar moment for the right interpretation of many morbid phenomena; I only want, with reference to the growth of organs, to establish a timely distinction between those organs which are made up of the connective substances, and that apparatus which supplies the necessary pabulum for *their* growth, as well as for that of the muscles, nerves, glands, &c. This "connective tissue" κατ ’ἐξοχην, must detain us for yet a moment while we consider how its corpuscles originate from embryonic cells. The form assumed by these corpuscles depends essentially on local conditions, upon the space available for their evolution. The great majority become spindle-shaped, corresponding to the elongated interstices left for their reception between the fibres of the connective tissue. Whenever the basis-substance allows them to expand freely in all directions (as in mucous tissue) they readily assume a stellate form, and anastomose with one another by means of their processes. Should they lie in the narrow fissures between fibrous bundles and lamellæ of larger size, they become flattened, forming epithelioid plates, or else they may continue, even in this flattened condition, to give off anastomosing processes, as in the cornea and *tunica intima* of the arteries. Thereupon a portion of the protoplasm very commonly stiffens into a homogeneous, colourless, highly refracting substance; we get stellate figures, plates, and fibres, which must be carefully distinguished from the plates and fibres of the intercellular substance; the necessary criterion being readily afforded by their chemical properties, inasmuch as they do not, like the intercellular substance, swell up and disappear on the addition of acetic acid. It sometimes happens (*ligamentum pectinatum*) that the entire cell, together with its nucleus, undergoes the metamorphosis in question. More commonly, however, the nucleus remains unaltered, together with a residual portion of granular protoplasm, occupying, as a rule, the centre of the stiffened cell. This is how the *stationary* corpuscles of the connective tissue originate; and in this state they remain during the whole life of the individual, unless they are roused to renewed activity by pathological irritation.

§ 75. We come now to the LYMPHATICS AND LYMPHATIC GLANDS. This is the third and last of the chief constituents of the intermediate apparatus of nutrition—the last in point of time, not in point of importance. It is only when the rate of embryonic development enters on a slower phase, after all the other organs have been mapped out, and even developed to some extent, that we can detect any lymphatics. Lymphatic glands are still later in making their appearance. This is undoubtedly connected with the function of the lymphatics, as drains for the removal of superfluous pabulum. So long as there is no superfluity of pabulum, inasmuch as it is all used up in the constructive process; so long as the outer coverings of the embryo are not too thick to check the free transudation of fluid, there can be no need of lymphatics. Contrariwise, we might predict that any obstacle to the escape of lymph must needs give rise to luxuriant growth of new tissue, to catarrhal and other secretions of all sorts from the affected surface; and this prediction would often be found to come true in the domain of pathology. *Recklinghausen's* beautiful researches into the lymphatics and the mode of their beginning in the tissues, have taught us that they are lined with precisely the same pavement of nucleated endothelia as the blood-vessels. This is also true of those still finer juice-canals which, according to the same observer, constitute the first beginnings of the lymph-path in the connective tissue, and communicate by minute pores with the apparently cæcal ends of the larger lymphatics. These canals generally present the form of flattened, stellate lacunæ, and are indeed, for the most part identical with those fissures and stellate interstices in which the flattened cells of the connective tissue (*Ranvier*) lie. As the lymphatics extend farther into the connective tissue, the minute communications with the juice-canals, alluded to above, become simply dilated (*Kölliker*); and this affords additional evidence of the homology between the connective-tissue corpuscles and the cells of the endothelium.

§ 76. The state of things as regards the glands is far harder to determine than as regards the lymphatic vessels. We are still in want of a thoroughly reliable account of their development. The older views of *Breschet* and *Engel*, who traced their evolution from plexiform knots of lymphatic vessels, have been lately reproduced, and that too in a form incomparably more plausible.* I feel obliged, however, to reject them. The specimens prepared by *J. Orth*† have led me to concur with him in holding that the first rudiment of a lymphatic gland is a collection of embryonic tissue, very highly vascularised, which forces its way between the fibres of the surrounding connective tissue, thereby forming for itself a capsule. It is only after this has taken place that a clear sub-capsular space appears at its periphery, and interstitial fissures become visible in its interior; the latter, by their connexions with the peripheric zone, partitioning the gland-substance proper into follicular cords and terminal nodules in the usual way. From a purely physiological point of view, the lymphatic gland presents itself as a local dilatation of the lymph-path, filled with a new and peculiar kind of tissue—the "lymphadenoid tissue." This is made up of lymph-corpuscles embedded in the well-known reticulum; it is held to be the great breeding-ground for the colourless corpuscles of the blood; and as it is generally agreed that the red corpuscles are evolved from the colourless ones, and that the migratory cells of the connective tissue are colourless corpuscles which have escaped from the vessels, the tissue of the lymphatic glands may be regarded as the common source of all the mobile cells of the entire intermediate apparatus of nutrition. Unfortunately however, this hypothesis, like many others on the genesis of tissues, still rests on an uncertain basis. We must admit that the lymph-corpuscles in the glands have hardly ever been seen to divide, the assumption reposing mainly on the old and readily demonstrable observation, that the lymph contains fewer corpuscles before its passage through the glands than after it. But may not this increase in the number of corpuscles be due to emigration from the blood-vessels? There seems to be no reason why leucocytes should not escape from the vessels in a lymphatic gland as well as in any other organ; nay, the very fact that the lymph-corpuscles are most abundantly generated during the digestive hyperæmia of the alimentary apparatus, in which, as we all know, the lymphatic glands take a conspicuous share, tells rather in favour of this theory than against it. For my own part however, I would rather not try, on such grounds as these, to overthrow the doctrine which has attained right of citizenship, and which is so very plausible *a priori*, that new cells originate in the lymphatic glands by fission of the lymph-corpuscles. I continue to regard the lymphatic glands as organs, which the intermediate apparatus of nutrition may be said to construct for itself, with a view to the renewal of its mobile cells; and it does this by causing the dilatation of circumscribed capillary areas at various points, followed by the emigration of colourless blood-corpuscles. The number of the emigrant cells subsequently increases by fission, and this increase continues to add to the bulk of the glandular parenchyma so long as efferent canals for the removal of the superfluous cells are lacking. At a later period a certain equilibrium is established between the production and the removal of the cells—an equilibrium which can only be disturbed by pathological irritants.*

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* *Sertoli* found that lymphatic canals lined with epithelium were first produced, that the connective tissue round them next underwent proliferation, and that corpuscular aggregates in this proliferated tissue were then developed into gland-follicles.

† *J. Orth*, "Lymphdrüsenentwickelung." Inaugural Dissertation. Bonn, 1870.

§ 77. The SPLEEN ranks with the lymphatic glands in its genetic history. The "formation of lymphatic sheaths," as the local emigration of colourless corpuscles and their accumulation round the vessels is usually termed—a phenomenon which my own observations have led me to adopt as the most probable mode of development of the lymphatic glands—is carried a step farther in the case of the spleen. In this organ, as in the lymphatic glands, the vessels begin by surrounding themselves with lymphatic sheaths, which here receive the name of Malpighian corpuscles. The vascular walls then undergo perforation, and split up into fibres. In this wise a delicate spongy tissue is formed, through which the blood percolates, to be again collected on the opposite side of the filter by efferent veins, which permeate the spongy tissue in all directions. The function of the spleen is environed by the same doubts and conflicting opinions as that of the lymphatic glands, save that the splenic pulp is held to be at once the birthplace of young leucocytes, and the grave of such red corpuscles as are growing old.

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* I cannot refrain from calling the reader's attention to the valuable analogies presented by the development of the lymphatic glands (as described above) to the many formative disorders of the intermediate apparatus of nutrition (*see* next chapter). In the latter as in the former case, migration of cells, followed by their fission, underlies all formative activity. Emigration brings the cells into *contact with the tissues*, and affords them a comparative measure of *repose;* and these conditions seem to determine first their amœboid motility, and secondly their fissiparous multiplication. I am convinced however, that fission rather than migration is the proximate and effective cause of inflammatory production and the growth of histioid tumours. To this is due the colossal size which these tumours may attain, such enormous increase depending on the inadequate development of the lymphatics, which are thus unable to provide, as they do in the case of the lymphatic glands, for the due removal of the excess of cells.

§ 78. So much for the genesis of the conjoint blood-vascular and connective-tissue system. We mark the distinction between its stationary and its mobile cells. To the former class belong what used to be called connective-tissue corpuscles, the endothelia of the blood-vessels and lymphatics, the stellate and anastomosing cells of the lymph-sinus and the splenic pulp, and finally the epithelia which line the serous cavities, since these are (according to *Recklinghausen*) in direct communication with the lymphatic system. The mobile cells are represented by the blood-corpuscles, and of these the colourless ones are peculiarly prone to accompany the nutrient fluid in its passage through the walls of the minuter vessels; after traversing which, some, as "migratory corpuscles of the connective tissue," place themselves at the disposal of the growing organs to be employed in the constructive process, while others make their way back into the blood through the lymphatics. The stationary corpuscles originate from the mobile cells; how the latter originate is still unknown. The cells in the parenchyma of the lymphatic glands and the spleen have the best claim to be regarded as their normal source. Yet if we bear in mind how the lymphatic glands themselves originate, we shall probably have to admit, as a fundamental postulate, that all colourless corpuscles, when once they have escaped from the circulating current, begin to migrate and to undergo division.

§ 79. Passing on to consider the growth of the remaining organs of the body, we will devote our first attention to CARTILAGE and BONE. Everybody knows that in sections of young cartilage the cells are (with hardly an exception) distributed through the matrix in groups, or at all events in pairs. The connexion of any two cells is evident from their each having a convex and a plane surface, the plane surfaces being opposed to one another. One is involuntarily led to think that they form the two halves of a globular body. That the appearances are really due to fission is shown from the occurrence of pairs of cells, which are still contained in a common capsule. Add to this visible proliferation of the cells, the intercalation of fresh intercellular substance which separates the independent halves of the divided cell to the proper extent, and we have the well-known scheme, according to which the growth of cartilage proceeds. I do not wish to cast any doubt upon the importance of these observed phenomena; but I must guard myself strenuously against being supposed to think that the growth of cartilage is provided for, even in major part, by this internal multiplication of cells and intercellular substance. Cartilage grows mainly by peripheric apposition. The perichondrium furnishes embryonic cells, which proceed to surround themselves with a layer of hyaline intercellular substance, which becomes continuous with the matrix of the existing cartilage. The oftener this process is repeated, the more cells does the cartilage contain. Those cells which were originally peripheric are gradully pushed towards the centre; and it is not till after this has occurred that the second factor in the growth of the cartilage comes into operation, *sc.* the gradual enlargement and subsequent division of the individual cells as they advance towards the centre of the mass. During this centripetal movement each element divides from one to three times. The division always occurs at the thickest part of the cell, in a plane at right angles to its long axis; hence the highly characteristic forms of the daughter-cells and their progeny. Half and quarter spheres, cones, &c., retain their peculiar shape throughout life, owing to the density of the matrix; for the same reason the cells which result from fission are never far apart, so that in the cartilages of an old man of ninety we may still observe those appearances which, when we saw them in young cartilage, led us to attach so high an importance to the internal growth of the tissue; in either case moreover we can determine with equal certainty whether the original cartilage-cell underwent fission once, twice, or three times, before assuming the final attitude of its repose.

Quite independent of the phenomena of normal growth, is a peculiar metamorphosis of hyaline cartilage, which we find (apart from morbid states) wherever the cartilage adjoins a growing bone. Whether the cartilage takes any active part in the development of bone, whether cartilage-cells, or even descendants of cartilage-cells, can be converted into marrow-cells or bone-corpuscles is still an open question. The metamorphosis now under consideration must however be regarded as a passive participation of the cartilage, in so far as it replaces the unyielding hyaline substance by a soft material, which offers no resistance to the extension of the osseous trabeculæ and the ingrowth of the medullary papillæ. The cartilage-cells again proliferate; and their proliferation, owing to the simultaneous liquefaction and partial reabsorption of the intercellular substance, assumes very considerable proportions. Each cell gives rise to from eight to sixteen very large daughter-cells. These are separated only by very thin trabeculæ of basis-substance, and form cylindrical columns, disposed at right angles to the surface of the growing bone. The vascular papillæ of the medulla penetrate into this soft, large-celled tissue as readily as though they were growing upon a free surface; they break down all partitions; and it is only where the form and position of the medullary cavity happens to allow it, that one or other of the stouter trabeculæ of the former matrix is retained as a sort of framework, on which layers of young bone-tissue are deposited. To conclude: here, as in sub-periosteal growth, the bone needs no antecedent condition for its development, beyond the presence of a vascularised embryonic connective tissue, which is everywhere produced upon its confines by the intermediate apparatus of nutrition, whether this be represented by medullary tissue or by periosteum. I will say no more at present about the growth of bone; ample opportunities for doing this will be afforded in the chapter on Diseases of the Osseous System.

§ 80. As regards the growth of the MUSCULAR ORGANS, we know that the first muscular fibres, whether smooth or striated, originate everywhere from embryonic cells. Where smooth muscular fibre is needed, the cells are converted into the well-known spindle-shaped or ribbon-like structures, while their nuclei assume the form of elongated cylinders (staff-shaped nuclei). In the case of striped muscle, the cells, according to *Kölliker*, increase in length, their nuclei undergoing repeated fission, until the proper length is reached. (According to other authors, each fibre results from the apposition of several cells.) The striped matter is then differentiated from the protoplasm, and becomes a cylinder whose diameter goes on increasing, while the nuclei are pushed to one side, where they combine with the residual protoplasm to form the muscle-corpuscles.

The after-growth of striped muscle consists, according to *Kölliker*, of a simple increase in the length and thickness of the existing fibres. *Weissmann* and *Kühne* describe in addition a peculiar splitting of the primitive tubes in the direction of their length. This phenomenon was studied by *Weissmann* in the muscles of the frog, by *Kühne* in those of rats and mice. The latter observer describes a marked increase in the number of nuclei and the quantity of finely-granular protoplasm at the points where the nerves enter. *Weissmann* saw the nuclei arranged in a row, dividing the contractile substance of the muscular fibre into two parallel bands. *Kühne* came across two muscular fibres in a single tube of sarcolemma. All these are facts which give us some sort of idea, though not a distinct picture, of the longitudinal splitting of the muscular fibre. Not a word is dropped by either observer suggesting any after-production of embryonic cells, destined for the additive formation of new primitive tubes. In disease matters take a different course. The repair of divided muscles by muscular tissue is indeed still very doubtful; beyond all doubt, however, is the regeneration of the muscular fibre in *myositis typhosa*, which we shall have to consider more fully hereafter. But in this latter case the phenomena are so complicated that we are unable to affirm with certainty that the regeneration is brought about exclusively by the mediation of embryonic cells.

We can speak more confidently about such organs as are made up of unstriped muscle. During *their* growth the cells increase in number as well as in length and thickness. Single fibres with forked extremities have often been met with in the walls of the pregnant uterus.* Inasmuch, however, as no multiplication of nuclei, no double nuclei, have ever been detected in these fibres, it remains very doubtful whether we are justified, on the above data, in assuming a fissiparous multiplication of the smooth muscular fibres. The doubtfulness of this hypothesis is enhanced by a positive observation of *Kölliker's*. He succeeded in tracing the origin and development of the muscular fibre through all its stages in one and the same specimen. (Cf. *Kölliker*, "Gewebelehre," 4te Auflage, page 567.) The embryonic cells required are furnished by the intermediate apparatus of nutrition, and are probably leucocytes which have emigrated from the vessels.

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* *Moleschott* and *Piso* in *Moleschott's* "Untersuchungen," vi. 1-6.

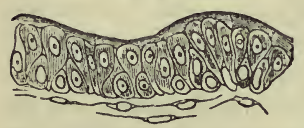
§ 81. As regards the NERVOUS SYSTEM, it has been generally believed hitherto that the growth of nerve-fibres was everywhere dependent on the pre-formation of embryonic cells. That the repair of divided nerves took place by the intercalation of embryonic tissue between the cut ends seemed finally agreed upon; indeed, it has not as yet been superseded by any fresh doctrine. On the other hand, a tendency has shown itself of late to refer the penetration of the nerve-ends into the growing parts of the body, and their consequent elongation, to an apical growth (Spitzenwachsthum) without any apposition of new elements. As regards the brain, *Besser* skilfully defends the position, that all the ganglion-cells of later growth exist pre-formed as so-called neuroglia-nuclei, in the very earliest stages of the development of this organ.

§ 82. One important question yet remains to be answered. How do the EPITHELIAL STRUCTURES grow and renew their losses? Unfortunately, no precise answer to this query can at the present time be given. We are justified, however, in provisionally adopting the following conclusions. A clear line must in the first place be drawn between those epithelia which grow *outwards* and those which grow *inwards.* The former invest the entire free surface of the organism, the skin and mucous membranes, forming an uninterrupted whole; the latter occupy certain cavities dug out of the parenchyma of the body, and are known as gland-cells or glandular epithelia. Both systems originate in the same layer of the blastoderm; throughout life they maintain this structural continuity, in such wise that the glandular epithelium may be regarded as a direct prolongation and inflexion of the surface-epithelium. Yet those who would comprehend the alterations of the tissues in disease must lay especial stress upon the fact that the antithesis in the direction of their growth alluded to above, exists from the very first, and that upon it is based the essential difference between the two systems. For the gland originates by the development of cellular protrusions from that side of the epithelial lamina of the blastoderm which is turned *towards* the conjoint blood-vascular and connective-tissue system: these protrusions divide and subdivide as they increase in length, and finally become hollow to a certain depth from the free surface. Their growth is decidedly central, and takes place by fission of the existing epithelial cells, which goes on repeating itself over and over again in the club-shaped ends of the processes. The intermediate apparatus of nutrition takes no part whatever in the process; nay, it is interesting to notice how it seems as it were to melt away before the advancing protrusions, contenting itself with the function of a mere stop-gap, the only function left open to it: it furnishes the interstitial connective tissue, the blood-vessels and the lymphatics, which, as we know, accommodate themselves humbly to the formal arrangement of the glandular tubuli, acini, &c.

§ 83. Matters take a very different course in the skin and mucous membranes. *Their* growth is regulated not by the epithelium, but by the conjoint blood-vascular and connective-tissue system, whose morphological elements (papillæ, membranes, &c.) determine the form of the surface, upon which the epithelium exists only as a tegumentary investment. This must be borne in mind when we find (in the course of the ensuing paragraphs) that the matrix of the surface-epithelium is situated, not in its own substance, but in the underlying connective tissue.

The cells of every epithelial stratum of considerable thickness exhibit certain characteristic variations in form, which may be viewed broadly as differences due to age—as phases of development. The youngest elements, remarkable for their small size, their softness and want of cell-membrane, are most deeply placed; they lie on the upper limit of the connective tissue. As we proceed outwards, the cells increase progressively in size, their membranous investment grows more and more distinct, they exhibit a more or less characteristic form. Their form is connected partly with variations in their function (cylindrical epithelium); it is partly due to a conflict between the forces which tend to make the cell grow uniformly in all directions, and the limitations of space which permit its growth to take place in certain directions only. A pregnant illustration of the results of this conflict is afforded by a vertical section through the epithelial lining of the urinary bladder (fig. 34). We can clearly distinguish three layers, each of which is made up of cells of a particular sort, differing characteristically from the other two. In immediate contact with the connective tissue is a single layer of small

FIG. 34.



The epithelium of the urinary bladder in section.

round elements; next to this we find pyriform cells of somewhat larger size, whose rounded heads are directed outwards, while their pointed ends dip down into the interstices between the round cells of the deepest layer. That these cells belonged originally to the deepest layer, that they were raised into the second layer by the propulsive force of cells of later growth, while remaining attached to their place of origin for a time by their inferior ends, this is an assumption which flows most naturally, as I think, from their pyriform shape. The cells of the third layer present, at first sight, the strangest peculiarities of form. They are flattened, and provided on their under surface with angular projections and shallow depressions which correspond to the heads of the cells of the second layer in much the same way as the *juga cerebralia* and *impressiones digitatæ* of the *tabula vitrea* correspond to the convolutions and sulci of the brain. These forms can only be explained by supposing that a cell, belonging to the second layer, is set free from its attachment to the connective tissue, that it protrudes towards the free surface, and that it is flattened and squeezed into the seams and irregularities of the second layer, by the centrifugal pressure of the urine which accumulates periodically in the bladder.

We cannot account so satisfactorily for the morphological variety exhibited by the constituent cells of every epithelium. Authors are unanimous, however, on one point, *sc.* that the epithelial cells appear everywhere to originate immediately upon the connective tissue, to be subsequently extruded from their original seat by the pressure of new elements. This unanimity however refers only to the *place*, and in nowise to the *mode* of origin of the cells. To explain the latter—omitting for the present to take *generatio æquivoca* into account at all*—two hypotheses lie open to us. We may either suppose the new epithelial cells to be produced by fission of the older ones, or to be extruded from the underlying connective tissue.

There seems to be no *a priori* reason why the cells should not originate in both ways. It must however be admitted that the epithelial cells have seldom been actually seen to divide. The mutual flattening of adjacent cells often misleads the observer into the belief that he has before him the results of fissiparous multiplication; the even line of contact between two cells presenting a deceptive likeness to a plane of division; hence the most conscientious vigilance on his part is in this matter indispensable. On the other hand, it is probable for many reasons that the young epithelium-cells spring from the connective tissue. *Burkhardt* was the first to indicate the topmost layer of the connective tissue as the matrix of the epithelial cells. When he described (in the year 1859) the way in which *he* believed the young cells to emerge from the connective tissue, and to assume an upright attitude as the youngest of the epithelial cells, many of his readers had scruples about accepting his results. Since that time, the migration of connective-tissue corpuscles has been directly observed by *v. Recklinghausen* in the cornea; and this observation gives colour to the view that the renewal of the epithelial cells is operated by a migration of their youngest elements from the connective tissue. The facts of morbid histology, so far from being antagonistic to this view, furnish many illustrations well adapted to shed light on the migratory process. I will only refer the reader to the interesting observations of *Biesiadecki* and *Pagenstecher*; in cases of slight and

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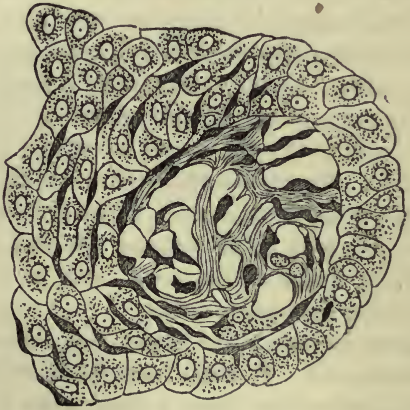
* *J. Arnold* (*Virchow's* Archiv, Bd. 46) has published some views on the regeneration of epithelial structures, which amount to a sort of *generatio æquivoca;* they are worked out with an amount of genuine care and research which render them worthy of the utmost attention.

Fig. 35.



Transverse section through a dermal papilla surrounded by epidermis. Migratory corpuscles may be seen both in the connective tissue and between the epithelial cells. After *Pagenstecher.*

superficial cutaneous inflammation (eczema and vesication) they detected migrating cells in all the younger strata of epithelium, cells precisely similar to other amœboid corpuscles visible in the papillary body (fig. 35). One fact, and one only, is being continually urged against this hypothesis—of the fact itself there can be no doubt—it is this: new epithelium, as *e.g.* after partial denudation of any epithelial surface, originates by preference, perhaps even exclusively in connexion and immediate contiguity with pre-existing epithelium. It would seem, therefore, since fission of the older elements cannot be shown to occur, that we are driven to assume that an embryonic cell can only develope into an epithelial cell when it is in contact with one of the latter kind. We must perforce adopt the theory of a sort of "*epithelial infection.*" This theory indeed would necessitate a twofold application; for supposing such infection to occur when embryonal cells, colourless blood-corpuscles, &c., are brought in contact with a permanent epithelium, it must likewise occur when, conversely, epithelial elements are brought in contact with a tissue composed of embryonic cells. The latter process indeed may actually be observed in the metastasis of cancer to lymphatic glands.

§ 84. This brings us to the end of our general summary of normal growth. We have seen, that apart from the first foundation of the various organs (from which we learnt that any and every tissue might originate from embryonic tissue), their actual growth depends but in small measure on fissiparous multiplication of their specific tissue-elements. We found this mode of increase in the gland-cells, in the fibres of striped muscle; to some extent also in cartilage; and we had grounds for suspecting that it also occurred in nerve-fibres. On epithelial surfaces there seemed to be need of an "epithelial infection," or at least of some sort of action of the older cells upon the immigrants. Everywhere else, the intermediate apparatus of nutrition, with its faculty of generating embryonic cells wherever required, sufficed of itself to maintain normal growth. It may be that it fulfils this function as a corollary of those obligations which are incumbent upon it in its nutrient capacity, allowing a certain number of colourless corpuscles to accompany the usual supply of fluid pabulum into growing organs, these corpuscles serving forthwith as materials for the constructive process.

§ 85. Entering on the domain of MORBID GROWTH, we meet first of all with a series of abnormal states, which may be defined simply as excesses of the normal growth of organs. These are either uniform enlargements, or partial protrusions or outgrowths, identical in texture and composition with the organ from which they spring; accordingly they only give rise to *quantitative* deviations from the normal standard of the affected parts. We indicate this fact in our nomenclature by the prepositions ὑπέρ and ἐκ, which common use allows us either to prefix to the name of the proliferating organ itself (*hyperostosis*, *ecchondrosis*), or to the word *trophia;* the latter term denoting in addition that the products in question are due to nutritive conditions of a peculiarly favourable kind (*hypertrophia*). It is best however, not to prejudge their mode of origin in this way; it is enough to express the simple fact by the words "*hyperplasia*, *hyperplastic.*" The hyperplastic states (conditions of overgrowth) of the various organs will be described in the respective chapters of the special division of this treatise. The position which they occupy in the domain of morbid growth is broadly but sufficiently indicated by what has just been said.

§ 86. All new formations which are not of a hyperplastic nature, involve a *qualitative* departure from the normal standard of development and growth. Hence it seems difficult at first sight to class them under physiological types. Our way is blocked, however, by obstacles of artificial origin, rather than by any which are inherent in the facts themselves; among the most important being the traditional habit of regarding the morbid deviation as something foreign (ἕτερον) to the organism, something introduced into it from without, of ascribing to it a parasitic life—even a kind of personality. This view, from which the term "heteroplasia" is derived, is justified in some measure by the two following considerations:—1. Those new growths which are due to the introduction of a definite poison into the body manifest themselves under similar forms in the most diverse organs (*e.g.* syphilis, tuberculosis, enteric fever). 2. The circumstance that each organ is the seat of election of certain special kinds of morbid growth, which always occur under the same form with but trifling modifications, so much so that when they have reached a certain point in their development, we are able to infer their character and future destiny from their situation. It is wrong, however, and prejudicial to the advance of real knowledge, when we allow the study and description of those features which are common to new growths in different organs to blind us to the right of each individual organ to have a morbid growth viewed as a disturbance of its *own proper* development—of its nutrition or of its degeneration. I must not be understood to question the utility, nay, the necessity of generalisations on the subject of morbid growth; but such generalisations ought rather to tend towards establishing the principles of development than towards the discovery of definite anatomical patterns on which any morbid growth—*e.g.* cancer—is constructed, in whatever organ it may occur. If I understand the times aright, men are weary of mere anatomical classifications based exclusively on outward characters. They will agree with me in thinking that the system has been brought into utter discredit by the inexhaustible variety of concrete forms. Henceforward therefore, while retaining the terms cancer, sarcoma, and so forth, and endeavouring to sketch in broad outlines the laws of their development and growth, without omitting to take their influence on the organism as a whole into account, we will always fall back upon the description of the individual forms in the Special Part of this work, and keep alive to the fact that a knowledge of these concrete forms is at least as important for the practitioner as a correct appreciation of those general features which they possess in common.

§ 87. Having done with this digression, let us resume the thread of our discourse, by seeking the cause of every deviation from the rule of normal growth—the cause of heteroplasia—in an over-activity of one or other of the two factors which cooperate in the growth of organs. The intermediate apparatus of nutrition has the first claim on our attention. Many products of morbid growth originate from this alone—*e.g.* interstitial inflammation, tumours made up of granulation-tissue, sarcomata. In a second series, the epithelium steps in to rival the conjoint blood-vascular and connective-tissue system, and we have many opportunities of testing the accuracy of our views of epithelial growth in the caricatures of it (Zerrbildern) presented by the various forms of carcinoma. It cannot be denied that this division of labour is prefigured in the physiological relation of the two systems to one another (as summarised in § 84). I cannot therefore be blamed for basing at least the main divisions of the subject upon it.

3. Products of Morbid Growth derived exclusively from the Intermediate Apparatus of Nutrition.

1. *Interstitial Inflammation.**

§ 88. When the organism is mechanically injured at any point, or exposed to any other sufficiently active source of irritation, the aggrieved part undergoes a series of changes, to the sum of which we apply the term "Inflammation." The name directs attention primarily to the important part played by the vascular system in the inflammatory process. The capillaries become congested; the affected part grows red and hot. It begins to swell; the swelling is to be ascribed partly to the over-distension of the vessels, partly to the escape of various constituents of the blood into the tissues. The "inflammatory exudation"—the material which escapes from the vessels, and infiltrates the tissues—is the more enduring product of inflammation, and claims our chief attention, owing to its important connexion with the course and issues of the process.

§ 89. The inflammatory exudation consists, apart from its fluid portion, of embryonic cells, which are characterised by the lively amœboid movements they exhibit. It was generally believed a few years ago that these cells were produced exclusively by proliferation of the connective-tissue corpuscles at the seat of inflammation. The dazzling picture, in which we thought we could distinctly appreciate the course of cell-multiplication, exhibited in the immediate vicinity of the inflammatory exudation, instead of the stellate corpuscles of connective tissue, first one, then two, then a progressively increasing number of round cells, arrayed in ranks, which grew longer in proportion as they approached the focus of inflammation, and finally mingled with one another. But now we know that a great majority of these cells are colourless corpuscles which have emigrated from the vessels. This is shown by an experiment of *Cohnheim's.* The mesentery of a living frog is stretched over a ring of cork, and subjected to direct inspection. We can see how the veins dilate; how the colourless corpuscles first adhere to their inner surface, and then put forth processes which penetrate their walls; how that portion of a process which has already escaped swells up, and forms a kind of bridge, along which the whole substance of the cell gradually creeps. Once through, the cells travel farther by the aid of their amœboid contractility; if a special point of the tissue is being irritated, that point becomes, in a general way, their goal. There they continue to accumulate; the result of their accumulation being a certain quantity of that very embryonic tissue which serves as the starting-point of all further changes (fig. 36).

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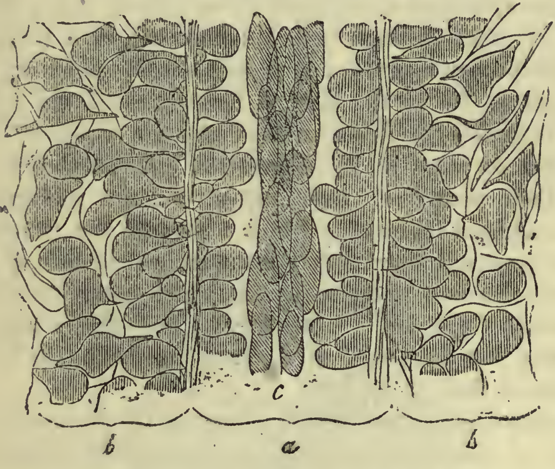
* *Interstitial,* as contrasted with catarrhal and parenchymatous inflammation, the former of which, so far as it concerns us, is an inflammation of mucous membranes (*see* Part II.), while the latter is identical with cloudy swelling (*see* § 36).

FIG. 36.



Cohnheim's experiment. *a.* Vein; *bb.* Adjoining connective tissue permeated by colourless corpuscles which have migrated from the vessel; *c.* Column of red corpuscles. $\frac{1}{500}$.

An older observation, which was first duly appreciated by *Billroth,* harmonises admirably with the above view of the development of plastic exudation or infiltration. It has been found that the vessels of inflamed parts are surrounded by a layer of young round-cells; and this holds good even of those vessels which extend far into tissues which have as yet undergone but trifling change. On the other hand, we can give a satisfactory explanation of the drawing, which represents "connective tissue undergoing proliferation," by assuming that it exhibits the colourless corpuscles "during migration," in which case they would naturally select the lines of least resistance, and therefore those interfibrillar channels which are normally occupied by the stationary corpuscles of the connective tissue.

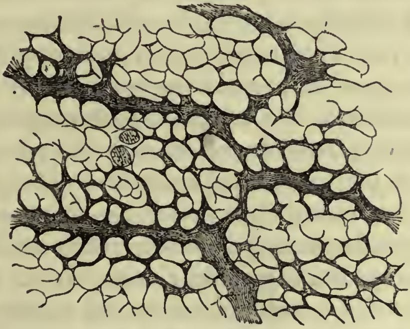
§ 90. The migration of the colourless corpuscles must not, however, be regarded as the *only* source of the inflammatory products. On the contrary the question, Whence can the blood obtain such a multitude of colourless corpuscles? leads to a series of considerations which tend to make us very chary of rejecting any possible sources from which these cells may be derived. On this ground we gladly welcome the beautiful researches of *Stricker*, which prove, at least with regard to the cornea, that a few hours after it has been irritated with lunar caustic, at a period when the colourless corpuscles can be experimentally shown not to have penetrated as far as the seat of inflammation, the stationary corneal corpuscles exhibit a series of changes which can only be interpreted as steps in a progressive metamorphosis. They retract their processes; their nuclei undergo multiplication; their protoplasm increases in bulk; between the fifteenth and the twenty-second hours they assume the appearance of mobile, multinuclear masses of imposing size, which remind us vividly of the so-called "giant-cells" (*see* § 67). It is but a step to the assumption that these may give rise to amœboid cells by a segmentation of their protoplasm.

The same author has directly observed the fissiparous multiplication of the emigrant-cells at the seat of inflammation. Concentrating his attention on the cells which appeared to be at rest just outside the vessels, he noticed on their surface certain lines of shadow, which came and went and shifted their position for a time, until at length a shadow deeper than the rest became stationary in the middle of the cell. At this point the little body became contracted; the contraction itself was more than once effaced; when it finally passed into a complete division, the two halves crept asunder in opposite directions. The denser the accumulation of cells, the oftener is this process of fission likely to be repeated, but the greater also will be the difficulty of tracing it under the microscope. And this perhaps is the reason why it has hitherto been often assumed to take place, but never distinctly demonstrated.

Our knowledge with regard to the source of the embryonic cells in inflammation is obviously in a transition state. But if we reflect that the doctrines advanced in the preceding section constitute the groundwork of all the remaining histological effects due to the "intermediate apparatus of nutrition," we shall perceive the immense importance to our scientific superstructure of every forward step in this department of inquiry.

§ 91. Continuing for a moment our consideration of the inflammatory exudation as a *fait accompli*, we must notice the remarkable influence exercised on the connective-tissue fibres by the cells to which they afford a refuge. *Billroth* has made some statements on this point which I think worthy of great attention. The fibres are not merely pushed asunder, but they undergo a certain degree of softening and fusion, so that instead of the tough web of which the cutis, even in its most delicate portions, is made up (*e.g.* in the prepuce), we find a delicate network which simulates the aspect of newly-developed intercellular substance (fig. 37), for which indeed it has often been mistaken.

Fig. 37.



Tissue of cutis rarefied by inflammatory infiltration: after *Billroth*. $\frac{1}{300}$.

Passing to the further histological metamorphosis of the plastic exudation, upon which, as already stated, the ultimate issue of the inflammatory process depends, we find three leading tendencies; the first towards Resolution, the second towards Organisation, the third towards Suppuration.

A. *Resolution.*

§ 92. It is clear that if our therapeutic skill availed to remove the cells which have migrated into an inflamed organ, that organ would return to the state in which it was before the inflammation set in. I put aside the alterations in the connective-tissue fibres described in the preceding section, alterations which might of course disappear with equal ease. The possibility of inflammation issuing in resolution, and the means of bringing about this issue, are questions therefore of the highest practical interest. The first measure which would suggest itself *a priori*, would be to help the cells to pursue the course they had already chosen, *i.e.* to let them migrate farther. Warmth and moisture would therefore be advantageous from this point of view. Elevation of temperature is known moreover to accelerate the movements of amœboid cells. When the inflammatory exudation is moderate in amount, and the irritant cause has ceased to operate, we may hope, by local elevation of temperature, to distribute the cells which have already migrated over a wider area, and to guide them gradually into the lymphatics.

The resolution of an inflammatory infiltration may also take place by fatty degeneration of its cellular elements. We have already seen how fatty degeneration converts cells of all kinds into a milky emulsion, to the reabsorption of which there is naturally no obstacle. A condition which appears to favour the commencement of fatty degeneration is the presence of fluid in abundance at the seat of inflammation. *Busch* has made the interesting observation that under the influence of cutaneous erysipelas some large sarcomatous growths underwent atrophy, and I had the opportunity of convincing myself in a similar case that the cells of the sarcoma succumbed to fatty degeneration. External warmth is well adapted for maintaining an enduring hyperæmia of this sort. Notwithstanding this twofold indication, great caution is requisite in deciding on the exact moment at which to substitute warm for cold applications to an inflamed part. The object of applying cold is to bring about an artificial contraction of the vessels, and so to check the progress of the exudation, to hinder the further migration of the colourless corpuscles. It is not till we have followed out this indication to the utmost, that we ought to resort to the application of warmth. Warmth is a two-edged weapon. What guarantee have we that instead of a dissolution of the exuded matters, which is of course our first object, there may not occur a greater concentration of amœboid cells at the heated point, *i.e.* suppuration and the formation of an abscess? Within certain limits, warmth acts as a resolving agent; beyond these, it stimulates the inflammatory process; in the former case it promotes the farther migration of the already exuded white blood-corpuscles, in the latter it helps to renew the migratory process, and adds to its intensity.

Note.—A therapeutic turn has been given to this section, to show the student how immediately the results of morbid histology may be brought to bear upon practice.

B. *Organisation.*

§ 93. Granting that the inflammatory exudation does not tend to resolution, the first alternative is its retention as a permanent constituent of the organic framework of the body. This retention is operated by the timely development of blood-vessels, and the conversion of the embryonic tissue into fibrillar connective tissue. The interstitial inflammations of internal viscera, which we shall hereafter meet with in the liver and kidneys, afford examples of this direct organisation on the largest scale. None of these examples can however be regarded as typical for the histological details of the process, because of peculiarities of local origin. The honour of serving as a type belongs exclusively to the process of repair in wounds, and primarily indeed to those which heal by first intention.

To illustrate the universal distribution of connective tissue throughout the body, I stated above, that no incision could be made without implicating connective tissue, without the presence of connective tissue on the cut surface. The truth of this proposition may be inferred from the consideration, among other processes, of the perfectly typical course of those phenomena which manifest themselves in the reunion of completely divided parts. These phenomena fall bodily under the head of inflammation, and are exhibited in precisely the same manner by the conjoint vascular and connective-tissue system, whether the wounded organ be the skin, or a muscle, or perchance the liver.

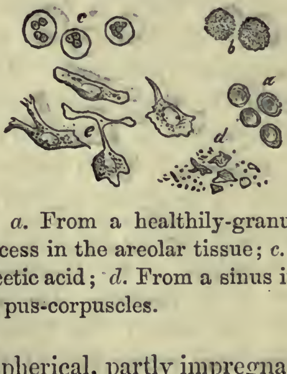
There certainly exists a mode of reunion which takes place with such extraordinary rapidity by the mere apposition of the cut surfaces, that no exuded material is required to complete it. The occurrence of this *immediate union* (*Macartney*) is confirmed by *Thiersch* in *Pitha* and *Billroth's* Manual of Surgery. It must therefore take precedence of union by first intention. In the latter mode, a substance is usually present which glues the edges of the wound together. It appears a very few hours after the injury, and proves, both at first sight and on more careful investigation, to be the connective tissue of the cut surface, infiltrated with blood-corpuscles and serum, and swollen by imbibition of the latter fluid. The next stage of the process consists in the migration of colourless corpuscles from the dilated vessels in the immediate neighbourhood. They permeate the whole of the cementing medium and the adjacent connective tissue, so that the divided parts are at length united by a continuous layer of embryonic tissue. The next step is the re-establishment of the circulation, which has been violently interrupted. This takes place as a general rule by the method of "secondary vascularisation" (§ 71), starting from those capillaries which are still pervious. *Thiersch* has recently furnished us with the details of the process. Should his interpretation of them be confirmed, they will materially extend our ideas respecting the development of new vessels in general. *Thiersch* found the cut ends of the vessels, a few hours after the injury, plugged by a corpuscular proliferation, and somewhat dilated, but seldom occupied by a blood-clot. Injecting the vessels at this stage with a warm solution of gelatin, and hardening the preparation in alcohol, he found: 1. Sticking to the surface of the club-shaped plug of gelatin, endothelial cells, some detached and isolated, others undergoing proliferation. 2. A peculiar configuration of the surface of the plug. This exhibited a number of thorny, seemingly broken-off spicula, which perforated the wall of the vessel, and proved on closer examination to be the radicles of a very beautiful system of intercellular canals, filled with gelatin. *Thiersch* sees in this system of canals a provisional nutrient apparatus, a preliminary vascularisation, and proceeds on this view to explain a fact which is certainly very énigmatical, viz. that even parts which have been completely separated from the parent organism may reunite with it, provided they are stitched on early enough. For us, the interest of his discovery lies first in the proof which it affords that the elements forming the walls of those vessels from which new capillaries are about to sprout have their cohesion relaxed in a definite way; and secondly, in the fact that his views corroborate the histological significance of the blood-vessels as "intercellular," not "intracellular" canals.

The last act in the process of repair by first intention, is the transformation of that portion of embryonic tissue which is not employed in the construction of vessels, into fibrous connective tissue. The cells first grow spindle-shaped, just as they do in the normal course of development; but, owing to their immense number, and the close way in which they are packed, this metamorphosis into spindle-cells gives rise to an entirely new variety of tissue—the *spindle-cell tissue.* This term denotes a texture wholly made up of parallel rows of spindle-shaped cells, which are held together by the dovetailing of their pointed ends. The spindle-cell tissue forms as a rule cylindrical or slightly flattened bundles, which interlace like the bundles of connective tissue. The only question is whether the protoplasmic substance of the spindle-cells undergoes direct transformation into gelatin-yielding fibres, or whether we are to assume with *Rollett* that the fibres are coined out of the intercellular substance. My own observations lead me to conclude that when cicatricial tissue is formed from spindle-cell tissue, the greater part of the body of the cell is immediately converted into the substance of the fibre. After a certain time, although the nature of the tissue is still recognisable in fine sections, it becomes impossible to isolate its component spindle-cells by teasing with needles; it tends rather to break up into stiff, fibrous fragments of irregular outline; and these, as is proved by their contained nuclei, are made up of cells which have become fused together. This phenomenon can only be explained on my view of the process. The fibrous bands of the cicatricial tissue are not merely the direct successors, in a general sense, but the *only* successors, of the fasciculi of the spindle-cell tissue. As contrasted with the normal development of areolar connective tissue, the entire process gives us the impression of a reckless expenditure of capital, where a judicious employment of the interest would have yielded far better results. I say emphatically, *better* results, for the cicatricial tissue is far from being a connective tissue of ideally high quality. On the contrary, its fibres are stiff, inelastic, and misshapen; its cells are represented by shrunken staff-shaped nuclei, and its vital capacity is proportionately reduced. Moreover, the cicatricial tissue exhibits an extreme proneness to contract in all its dimensions. This phenomenon, which is, on the whole, a very mischievous one, is termed induration, sclerosis, or contraction; its occurrence is anticipated with such certainty, that upon it is founded the operation for entropion, by which an inverted eyelid is turned outwards. It need hardly be said, that this general diminution in bulk is a physical rather than a vital phenomenon; the removal of water has a great deal to do with it; for the white, glistening tissue of a cicatrix is dry, compact, and harder to cut than any other variety of connective tissue.

c. *Suppuration.*

§ 94. Pus is a fluid tissue. Numberless cells, the so-called pus-corpuscles, are suspended in a colourless serum to which they impart a greyish-white or yellowish-grey tint; the *liquor puris* holds albumen, mucin, pyin, and salts in solution. The cells are small and spherical, partly impregnated, partly sprinkled with fine granules which, as a rule, conceal the nucleus from view. On the addition of acetic acid the granules disappear,

Fig. 38.



Pus-corpuscles. *a.* From a healthily-granulating wound; *b.* From an abscess in the areolar tissue; *c.* The same treated with dilute acetic acid; *d.* From a sinus in bone (necrosis); *e.* Migratory pus-corpuscles.

and the nuclear structures start into clear relief. There is usually more than one nucleus; often three or four. In the latter case, the nuclei are small, not always strictly circular, and exhibit a peculiar lustre which suggests the homogeneity of their structure (fig. 38). These cells were at one time considered to be of specific nature, and were hence termed pus-corpuscles. This was an error; for we meet with similar cells in the blood, where a certain number of the colourless corpuscles are multinuclear; and with regard to these, *Virchow* declares that they are incapable of taking any farther part in the development of the blood. More recently it has been shown that saturation of the blood with carbon dioxide causes all the uninuclear colourless cells to become multinuclear and then to undergo disintegration. The presence of several nuclei has not the same significance here, as that division of the nucleus which precedes the fissiparous multiplication of cells; it seems rather to point to a breaking-up of the cell, preliminary to its total dissolution. Moreover, it is a mistake to suppose that pus contains only cells of this kind. Creamy pus indeed (*pus bonum et laudabile*), such as is poured out on surfaces clothed with healthy granulations, contains a large majority of uninuclear cells, which I should not be able to distinguish from the migratory corpuscles of connective tissue. Sanious pus, on the other hand, such as is yielded by carious bone, contains, as a rule, cell-derivatives, oil-globules, albuminous molecules, &c., rather than pus-cells. In fact, we find a series of transitional forms between the uninuclear and the multinuclear elements of pus, just as in the case of white blood-corpuscles; the latter, incapable of further development, undergoing disintegration by fatty and granular metamorphosis. According then as the pus is fresh or stale, according as it has been rapidly or slowly produced, or has undergone a slower or more rapid decomposition, do we find in it uninuclear or multinuclear cells or even cell-*débris*.

§ 95. When we hear it asserted that pus may be produced in various ways, when we find pus-formation in connective tissue, such as we have just now been considering, contrasted with pus-formation on mucous and serous surfaces, or in coagulated blood, &c., we must, in the present state of our knowledge, accept such contrasts with a grain of salt. The great bulk of pus is everywhere formed by the migration of colourless corpuscles from the vessels. We must bear in mind however the following points of divergence: first, the path taken by the migrating cells tends in the one case towards a free surface, in the other, towards a point situated in the parenchyma of the connective tissue; secondly, that in the development of pus on mucous and serous membranes, the share taken in its production by the epithelium must not be left out of account. As regards the formation of pus in connective tissue, *i.e.* the suppuration of an inflammatory exudation, with which alone we are now concerned, we must keep in mind the same reservations and restrictions which we were obliged to establish in connexion with the process of plastic exudation itself. It is by no means proved that all pus-corpuscles are derived from the vessels; for on the one hand a formative irritation of the stationary corpuscles of connective tissue has been shown to take place, and their break-up into migratory cells rendered highly probable; while on the other hand, multiplication of the exuded cells by division has been directly observed. Finally, we may look on suppuration as in reality the most direct continuation of the earliest phenomena of inflammation. Its essential feature is a tendency towards over-production, towards exuberance of growth, whereby colossal numbers of young cells are generated in a relatively brief period of time. The proximate cause of the suppuration of an inflammatory exudation, or, in ordinary phrase, of the passage of inflammation into suppuration, is often to be sought in the excessive afflux of pabulum to the inflamed part; hence the antiphlogistic method of treatment endeavours in the first place to moderate or diminish this afflux. In other cases again, we find the cause in the *quality* of the irritant; thus chemical agents, and particularly septic ferments, lead to suppurative inflammations. Conversely, we might anticipate that in individuals whose nutrient fluids had undergone septic infection (septicæmia), every inflammation would tend to assume a suppurative character. Finally, there is such a thing as individual predisposition, *i.e.* there are persons in whom the most gentle irritants excite suppurative inflammations. But this is by the way. We must return to the consideration of the anatomical course of the suppurative process.

§ 96. The next phase is the formation of an *abscess*. The cells which were originally distributed with tolerable uniformity through the inflamed parenchyma, forsake their seat of origin, and make their way from all sides towards a central point, which subsequently becomes the purulent deposit (*abscessus*, *apostema*). This migration is due partly to the spontaneous motility of the cells, partly to a more or less vigorous transudation from the vessels, which assists their transit and determines its direction towards a common centre. After this convergent current has been flowing for a time, the centre in question exhibits a nodular induration. In its interior the vessels are compressed, the parenchyma grows pale, the nutrition of the part ceases with the arrest of the blood-supply; softening and fatty degeneration set in; in the transuded fluid the fibres of the connective tissue melt away, and the cells are freed from their connexions. Fluctuation is now perceptible to the finger; the purulent deposit is formed, or, in surgical phrase, the abscess is ripe.

Having thus traced the development of an abscess, it seems hardly necessary to define it as an interstitial cavity in the body containing pus, were it not that purulent accumulations may arise in other ways as well; these indeed are not termed abscesses, but they are equivalent to abscesses in a histological point of view; I allude to purulent effusions into closed cavities, such as serous sacs, joints, mucous bursae, and sheaths of tendons. This extended application of the term corresponds to very wide limits of variation in point of size and form, but it finds its justification in the identity of their subsequent course.

§ 97. By far the most frequent termination of an abscess is its rupture, the evacuation of the pus externally. The same forces which brought the pus together continue to push it forward in the direction of least resistance. The elastic reaction of parts which enclose the pus, and which it has displaced, operates in the same way; and as the pus (thanks to the very extensive distribution of the connective tissue) is everywhere in contact with a tissue susceptible of being itself converted into pus, the pre-eminent frequency of this termination is quite intelligible. The pus then forces its way in the direction of least resistance; this direction is in the last resort always outwards, the final result being perforation of the cutis, or of a mucous membrane. The matter once evacuated, the cavity of the abscess becomes a free pus-secreting surface; it falls under the category of ulcers, which we shall presently have occasion to consider.

§ 98. But the pus is not always discharged externally. Nay, it may be made capable of reabsorption, at any stage of its accumulation, by fatty degeneration of its corpuscles, and so be absorbed. Moreover, some recent observations make it likely that this capacity for being reabsorbed belongs even to abscesses of old standing which have become cheesy, and whose size has continued the same for long periods of time. The cheesy matter enters the blood-vessels and lymphatics in a minutely particulate form, and may then (as we shall see hereafter) give rise to miliary tuberculosis.

D. *Organisation after Suppuration.*

§ 99. The sum of all that has already been said concerning the nature of pus shows clearly enough, I believe, that this product is something alien, something which has become foreign to the organism, and against which it is not guarded by a protecting coat of epithelium as it is against the outer world generally. From the moment, therefore, that the abscess is constituted as such, the organism tends to restore its own internal unity and completeness (Insichgeschlossensein) which are disturbed by the presence of the abscess. To this end however the simpler means of organisation referred to above, *sc.* the production of vessels and connective tissue are not of themselves adequate. A new skin and cuticle have to be formed; and this brings us to that most interesting variety of morphological evolution which is usually termed *repair by second intention.* The term is primarily applied to the healing of wounds, when we have failed to restore the solution of continuity by precise apposition of the divided parts, when suppuration has compelled us to remove our sutures and strapping, or when the loss of substance is so great that the due approximation of the cut edges is impossible, and the parenchyma is left unprotected, exposed to the action of the atmosphere, &c. Here too, however, the denotation of the term transcends its definition. Exactly the same phenomena recur when the organism has to be shut off from an abscess, or anything analogous to an abscess (§ 96); when a portion of the body has been converted by necrosis, burning, or corrosion into a foreign body, only to be got rid of by suppuration. To this group too belongs the process of repair in ulcers; in a word, repair by second intention is synonymous with organisation after suppuration.

§ 100. We have to do with a free surface yielding pus. From countless points of this surface young cells are forcing their way; these are accompanied by a fluid mainly transuded from the blood, and very rich in dissolved albuminous matters. Sooner or later the frontier-line of the secreting surface exhibits changes diametrically opposite to those which occurred when the plastic exudation melted into pus. The cells close up their ranks. A layer of embryonic connective tissue is formed, which intervenes between the parenchyma of the organism on the one hand, and the pus on the other. Any pus-corpuscles which may be secreted after the completion of this membrane must make their way through the layer of embryonal connective tissue; this waxes thicker, and rises into small globular protuberances, the so-called "fleshy warts," or "granulations." These granulations are the physical basis of all further evolution; they produce both skin and cuticle, but before all, new vessels.

§ 101. *Vascularisation*, here as elsewhere, is the most powerful agent in organisation. The reason why the massing together of cells in large numbers is associated with increased frailty of the individual elements, lies in the great difficulty with which an abundant collection of cells, *e.g.* the pus-corpuscles which unite to form an abscess, can be supplied with nourishment, if indeed their nourishment is possible at all. Should the collection be a large one, the elements nearest its periphery will continue to get what pabulum they require from the adjoining nutrient fluid, and to rid themselves of their excrementitious products. The farther we advance inwards the greater do the obstacles in the way of this interchange become; the excreta accumulate; the pabulum has no access to the parts. The only way in which these disastrous results may be avoided is by vascularisation, *i.e.* the formation of canals, through which the products of the organs of sanguification may be carried into the midst of the territory requiring nourishment, and the excrementitious matters from the interior of the same territory may be removed. In this way even aggregates of embryonic tissue of considerable size may persist for some length of time, and maintain their connexion with the organism.

§ 102. As regards vascularisation, in the course of repair by second intention more particularly, the distribution of the embryonic tissue upon a level surface affords favourable opportunities for the access of pabulum. Nevertheless, an abundant development of new vessels sets in here at a very early period to promote this object. The histological details of the process are the same as in the secondary mode of vascularisation; along certain lines running through the parenchyma which is to be vascularised a closer aggregation of the cells becomes apparent; a cord or row of cells becomes visible, pointing out the form and direction of the future blood-path. But how is a cylinder of cells converted into a tube? How is the new vessel opened up? These questions can only be answered by a reference to the discoveries of *Thiersch*, alluded to under the head of repair by the first intention. Since the pervious parent-vessels, on which both limbs of the newly-formed loops rest, are also shrouded in a dense mass of cells, the most enigmatical part of the entire process is withdrawn from direct observation. We know that at a certain time the blood makes its appearance in the axis of the cellular cord, that the cells of which the latter consists are pushed asunder by the stream, and proceed forthwith to form the wall of the new vessel. I presume that the cells of which the wall of the parent-vessel is made up are everywhere loosened by the inflammatory irritation, thus ceasing to offer any special hindrance to the tunnelling of a channel for the blood. Some such hypothesis is indispensable for the due appreciation of the farther progress of vascularisation, during which the newly-formed vessels, which are still wholly made up of cells, give rise in their turn to new vascular loops. The development of capillaries from within keeps pace with the formation of layer upon layer of new embryonic tissue upon the surface. The capillary loops, with their long parallel limbs, struggle vertically upwards into the granulations; they reach nearly as far as the suppurating surface, their points of curvature being somewhat dilated (fig. 39).

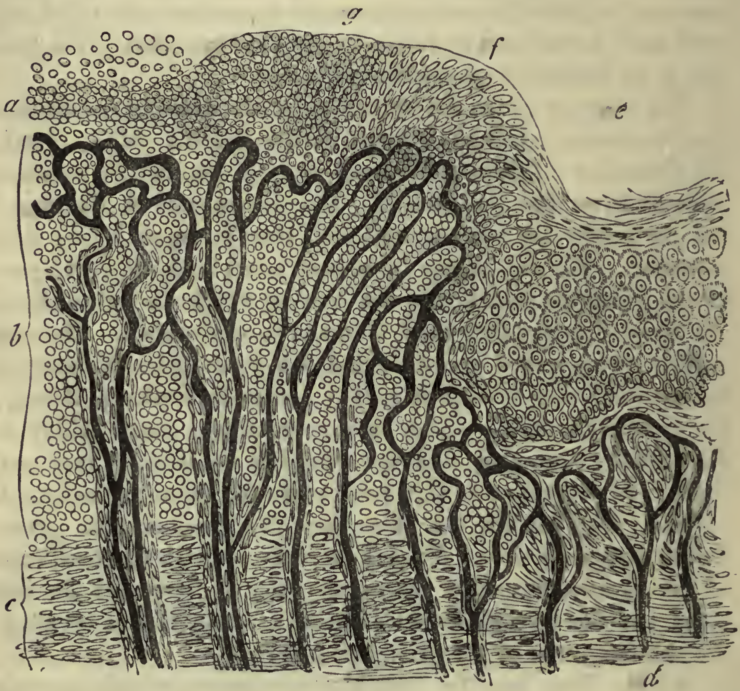
§ 103. This brings us to the point at which the formative process is most luxuriant. Supposing progress in this direction to be unrestrained, it may lead to another morbid deviation, *sc.*

to the formation of the so-called "proud flesh" (*caro luxurians*), whereof more anon. As a rule however, a farther change now occurs which is suited to check any excess of production on the affected surface, and to pave the way for cicatrisation. The embryonic connective tissue undergoes conversion into cicatricial tissue. The change begins in the deepest layers of the granulations, and exhibits the same phases and transitions with which we were made acquainted in repair by the first intention. The first step is the formation of spindle-cell tissue.

The plane in which the spindle-cells are stratified determines the direction in which the earliest fibrillæ become visible. Next, the formation of cicatricial tissue and its contraction succeed each other, as described in § 93. The phenomenon is the same; but the results are more complicated than in repair by the first intention. For as it begins (as already said) in the deepest layers of the pyogenic membrane, the base on which the granulations are situated is the first part to undergo contraction. The raw surface shrinks; and it is the vessels which are primarily affected by this shrinking, inasmuch as they penetrate vertically through the cicatrising base. They are compressed, their calibre is diminished; nay, they undergo complete obliteration here and there. In proportion as this takes place the granulations lose in volume, they contain less juice, and the pus-formation grows feebler and more slow. Thus, by a really astonishing consilience of the various formative forces, the way is paved for the last step; and this consists in the secretion of an epithelial covering, the skinning over of the granulating surface.

§ 104. True that the cuticular investment usually spreads from the edges of the granulating surface towards its centre. To this rule however there are exceptions; small patches of cuticle have often been noticed at some distance from the edge, patches which gradually increased in size and finally blended with the marginal skin. Even were there any difficulty in determining this fact with the unaided eye, all doubts would be removed by carefully examining a vertical section through the edge of a granulating surface in process of repair (fig. 39); this shows conclusively that the raw surface gets its cuticle not by an independent ingrowth of the epithelium from the edges over the granulating surface, but by the conversion of the outermost layer of the granulation-tissue into epithelium. At *e* (fig. 39) the separation of the epithelium from the connective tissue is complete, at *f* the boundary-line is blurred, but even at *g* we are still able, by the closer arrangement of the outermost cells to recognise the future epithelium, although no differentiation of the elements, as regards their size, the character of their nuclei, &c., has yet set in. We come next to the suppurating surface; it would seem as though the first foundations of the epithelium

FIG. 39.



Vertical section through the edge of a granulating surface in process of repair. *a.* Secretion of pus; *b.* Granulation tissue (embryonic tissue) with capillary loops whose walls consist of a layer of cells longitudinally disposed; their thickness decreases as we approach the surface; *c.* Cicatrisation beginning at the base (spindle-cell tissue); *d.* Cicatricial tissue; *e.* Fully-formed cuticle—its middle layer consisting of grooved cells; *f.* Young epithelial cells; *g.* Zone of differentiation. $\frac{1}{300}$.

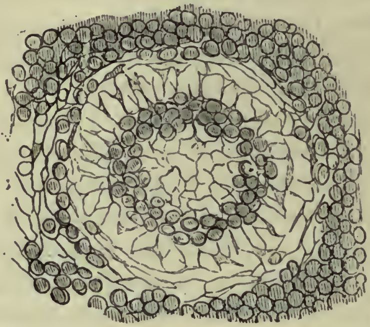
were laid by pus-corpuscles which had not been set free. If we look for something analogous to this mode of epithelial development, we can only compare it to the primordial separation of the blastodermic tissue into epithelial and non-epithelial strata, and so regard it as a true embryonic differentiation. The adjoining normal epithelium obviously cannot be deemed inert in the matter; it must be considered to exert some sort of "epithelial infection" (§ 83). Indeed some such hypothesis is necessary to explain the greater frequency (according to *Heine* and *Billroth* the invariable occurrence) of cuticular cicatrisation from the margins. The newly-formed epithelium always remains thin and dry. It has never been hitherto observed to develope regular glands or hairs; on the other hand, I am able to state from personal knowledge that in some cases of epithelioma in scars, the peg-shaped protrusions of epithelium characteristic of this form of tumour start from the thin cuticle of the cicatrix.

§ 105. These are the outlines of formative inflammation, when this runs its entire course in the intermediate apparatus of nutrition, and is combated by its means alone. Various modifications of great interest and importance are determined by the peculiar structure of the individual organs, and must therefore be reserved for consideration in the Special Part of this work. In this place I will only allude once more to that singular deviation from the normal course of repair by second intention which consists in the growth of the so-called "proud flesh."

The *caro luxurians* may be defined as an overgrowth of the granulations. Instead of little warty prominences, which ought not to exceed a line in height or in breadth, we have fungous masses cropping up, characterised by being three or four times larger than ordinary granulations, partially dendritic in form, highly vascular, and possessing a certain power of resisting external influences. These fungous granulations are distinguished histologically by a peculiarly high degree of differentiation of the embryonic tissue. In the first place, we have a more elaborate stroma throughout, a stroma resembling that of the lymphatic follicles. It is formed partly by the interstitial cement of the connective tissue, which fills up the lacunar network between the spheroidal cells: this stiffens into fine cylindrical threads: partly by a certain number of the cells themselves. These assume a stellate form, and constitute the nodal points of the stroma at tolerably uniform intervals. This stroma can only be demonstrated by carefully pencilling out a fine section of granulation-tissue hardened in alcohol.

This arrangement constitutes of itself a structure of a higher order, comparable in some degree to the connective-tissue stroma of the intestinal mucous membrane; and the analogy is carried farther by the occurrence of certain spheroidal bodies which I must pronounce to be newly-developed lymphatic follicles (fig. 40). These lie in the midst of the parenchyma, equidistant on every side from the greater vessels. We can readily convince ourselves, by examining very fine sections which have been pencilled out, that these round nodules consist mainly of a very delicate reticulum in which minute lymph-corpuscles are embedded. The lymph-corpuscles are more firmly attached to the reticulum towards the periphery of the nodules than in their centre; so that we usually have a border-zone, which it is difficult to clear up. Beyond this we find a zone, traversed by stellate corpuscles of considerable size; so that if we could only prove that these structures were in communication with the lymphatic vessels, the evidence in favour of their being true lymphatic follicles would be complete. I may remind the reader that this communication still remains to be proved in the case of the tonsillar follicles as well.

FIG. 40.



Lymphatic follicle from a fungous granulation (Caries fungosa). For explanation *see* text. $\frac{1}{300}$.

§ 106. Nerve-fibres are not an integral constituent of granulations; yet surgeons are familiar with so-called "irritable granulations," and I have succeeded in discovering an abundant supply of nerve-fibres in an exquisite example of these sent to me by Professor *Billroth.*

2. NON-INFLAMMATORY OVERGROWTH OF THE CONNECTIVE TISSUE.

§ 107. I have already (§ 85) relegated the hyperplastic conditions of individual organs to the corresponding chapters of the Special Part of this work, inasmuch as from a histological point of view they do not furnish materials for any generalisation save only that they are quantitative excesses of normal growth. Now the interstitial connective tissue forms an exception to this rule, because it is only a constituent of the various organs, and not itself an organ, and because its increase by way of overgrowth must therefore necessarily entail a qualitative change in structure. Strictly speaking, a large proportion of the processes included in the domain of interstitial inflammation may also be viewed as consisting in an overgrowth (hyperplasia) of the interstitial connective tissue. This applies especially to inflammatory infiltration and the conversion of the infiltrated products into connective tissue. In point of fact the non-inflammatory differs from the inflammatory form of overgrowth only by its slower rate of progress, if we set aside for a moment all thought of its causation. A hyperæmic dilatation of the vessels constitutes in every case the starting-point of the morbid process. This is associated with an emigration of colourless blood-corpuscles, which gives rise to an increase in bulk, a thickening of the connective tissue. Especially noteworthy is the extent to which the sheaths of the vessels are infiltrated; they often attain from three to five times their normal thickness. The transformation of the infiltrated cells into fibrillar connective tissue is a work of time, and seems in many cases (kidneys, pia mater) not to occur at all. Meanwhile the close analogy between this process and inflammation is self-evident, so that we cannot quarrel with authors and practitioners for continuing to call it "chronic inflammation." Wherever a definite source of irritation, *e.g.* a persistent or often renewed, though feeble mechanical irritant is the cause of the disturbance, I too am ready to call it "chronic inflammation"; but where this is not the case, where, *e.g.* the phenomena in question are due to passive congestion, it would be utterly wrong to go on speaking of an inflammation instead of a simple hypertrophy or overgrowth.

3. SPECIFIC INFLAMMATIONS.

(*Granulomata and Lymphomata.*)

§ 108. As the present chapter will introduce us for the first time to the hackneyed word "tumour," it is needful that we should give some brief account of its denotation and significance. As practitioners we incline to call any new growth a "tumour" in proportion as it lacks the known characters of the inflammatory process. Thus:—1. The less evidence there is of its having been caused by an inflammatory irritant, the more does the new growth exhibit a character of "spontaneity." Here of course, as everywhere else in nature, no such thing as real "spontaneity" is possible. But we are still so far from having any clear insight into the etiology of tumours, that it is really a matter of choice whether we follow those who regard the tumour as the localisation of an antecedent dyscrasia ("Geschwulstkrankheit"), or those who consider the local mischief to be in every case the starting-point of the general disease. *Billroth*, in his Manual of General Surgical Pathology, has taken the former view; while *Virchow*,* in his book on Tumours, adopts the latter. With amazing care, *Virchow* endeavours to prove the existence of at least a local predisposition in each single case; and although he has not succeeded in driving the arguments of humoral pathology wholly out of the field, he compels us to admit that some tumours at least originate in a local irritation. As examples we may take epithelioma of the lower lip, due to the persistent irritation of a tobacco-pipe held between the teeth; so also a number of sarcomata caused by pressure; enchondromata of the bones starting from the seat of fractures, &c. Again—

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* *Virchow* (Krankh. Geschwülste, vol. i. p. 121) divides tumours resulting from proliferation of tissue (as opposed to cysts, &c.), into:

1. *Histioid;* made up of some one tissue normally present in the body (Sarcoma).

2. *Organoid;* made up of several tissues characteristically arranged to form an organoid structure; *e.g.* connective tissue and epithelium in the glandular cancers.

3. *Teratoid;* made up of several organoid elements, corresponding, however imperfectly, to an entire system in the healthy organism (Dermoid of ovary).

4. *Compound or mixed;* made up of various dissimilar parts or tissues, not conforming to any plan of normal structure (Cystosarcomata, &c.).—TR.

2. The less decidedly the remaining cardinal signs of inflammation, such as pain, redness, rise of temperature, are associated with the growth, the more nearly does it approach the nature of a tumour. The practitioner's attention is roused and he is led at once to suspect some inflammatory complication, when a tumour causes pain, or when an active hyperæmia with rise of temperature accompanies its development.

3. The less a new formation contains within itself the conditions requisite for perfect recovery, the less does it participate in the nature of inflammation. Spontaneous cure is a very distinctive peculiarity of inflammatory processes. Our conception of a tumour implies that it should continue to grow if left to itself; and even should its size remain stationary, that it should at all events exhibit a certain degree of permanence. This proposition may be formulated in conjunction with (1) in some such terms as these: inflammations do not originate spontaneously, though they get well of themselves; tumours arise spontaneously, but are not susceptible of spontaneous cure. I am well aware that such a formula as this is very far from being axiomatic. Pedunculated tumours are often spontaneously detached; nay even the spontaneous expulsion of entire nodules of cancer has been known to occur.

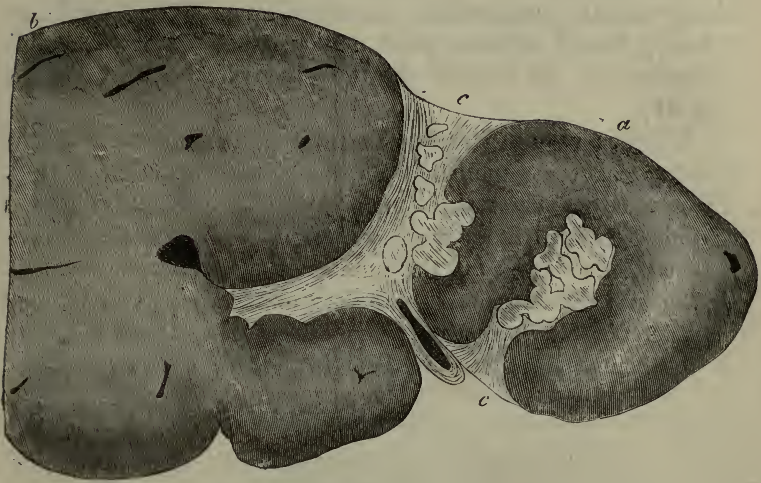
If we inquire into the natural grounds of this distinction, almost instinctively applied by the practitioner, we find them in the circumstances of histological development. Inflammatory products are generated at the seat of irritation mainly by the accumulation of the mobile cells of the conjoint vascular and connective-tissue system; this accounts for the rapidity with which they appear, and for hardly a trace of their presence being left when they disappear; the development of tumours is more nearly in accordance with the laws of normal growth;

hence their permanence and quasi-organic character. Bearing in mind that an increased afflux of blood plays a chief part in the phenomena of inflammation, we might designate inflammations as disturbances of nutrition, tumours as disturbances of growth. Nevertheless, the opposition is one not of contradictories, but of contraries only, which are connected by several series of intermediate members. One series conducts from inflammation through the intermediate phases of inflammatory overgrowth and simple overgrowth to those more complex forms of overgrowth which we call cancers. Another leads from simple inflammation through specific inflammation to those more perfect imitations of normal tissue, which we call sarcomata, enchondromata, myxomata, &c., and which, taken together, form the histioid group. The former series is chiefly exemplified in the disorders of the skin, mucous membranes, and glands; the latter will be dealt with at once.

§ 109. The specific inflammations differ from ordinary inflammation in that they furnish either instead of, or together with the plastic exudation, certain products which exhibit special anatomical peculiarities. These are typical for each individual form, and may be referred broadly to the special quality of the inflammatory irritant. This irritant is in every case a *specific virus*, which may be introduced into the organism either by hereditary transmission or by contagion, or primarily developed in the organism itself.

§ 110. Syphilis. Constitutional syphilis maintains a tendency in the body to every morbid change that comes under the head of active hyperæmia, inflammation, and inflammatory growth. In the earliest stages of the disease it is the more superficial organs, the skin and mucous membranes, which are chiefly affected; in the later stages the deeper parts become involved as well; we shall come across examples of syphilitic inflammation when we come to treat of the morbid anatomy of the osseous and nervous systems, of the liver, and the testicle. These inflammations are all distinguished by certain peculiarities in their localisation, their distribution, and their course. One product however merits our especial notice; it seldom occurs alone, but is usually associated with the simpler forms. I refer to the syphilitic gumma (syphiloma, *Wagner*). The gumma may be termed a specific product of syphilis; its specific anatomical character residing not in any marked deviation of the gummatous tissue from the familiar types of inflammatory

FIG. 41.

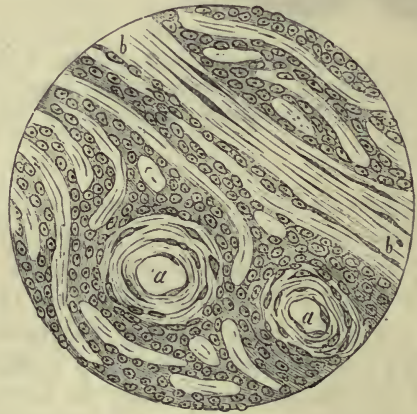


Syphilitic disease of the liver. *a.* Left lobe; *b.* Right lobe; *cc.* Fibroid sheath which traverses the organ from the V. portæ to the ligamentum suspensorium and contains gummata. $\frac{2}{1}$.

growth, but rather in the circumscription of a more or less spheroidal nodule in the midst of a larger deposit of newly-formed embryonic tissue, a nodule which differs from the embryonic tissues round it in the farther course of its metamorphoses. For while the latter undergo conversion into fibroid tissue, forming a cicatrix characterised by a tendency to extreme contraction (§ 93), the former, retaining the circular form of its cells, and occasionally producing an anastomotic network of corpuscles, undergoes a mucoid transformation of its intercellular substance. The main stress however must not be laid on the production of mucous tissue, inasmuch as this is clearly a mere phase in a slow degenerative change. The cells grow fatty; their place is taken by round or stellate aggregations of fat-granules, which appear to be capable of lasting as such for long periods of time. The final result is a yellowish-white rounded nodule of a soft and elastic consistency, embedded in a deposit of newly-formed connective tissue; this is the specific tumour of syphilis, the "tophus" or "gumma syphiliticum." The complete absorption of recent gummata may be effected by suitable medication. At a later period, the nodule becomes cheesy and the surrounding connective tissue is converted into a tough, fibroid cicatrix, which may occasion the most extreme distortions of the affected organ by its subsequent contraction (fig. 41).

Whether we are justified in calling the induration of the primary chancre gummatous I will not take upon me to say. The appearances presented (fig. 42) are those of an infiltration of the connective tissue with small cells, an infiltration distinguished not so much by the number of the infiltrated cells as by the fact that these cells are very uniformly packed into all the interstices between the vessels on the one hand, and the fibres of the connective tissue on the other. This causes an elastic tension, giving the finger a sense of hardness, while the vessels remain pervious and the nutrition of the parts is not interfered with. This invariable arrest of the cellular infiltration at a certain stage has undoubtedly something peculiar about it, and reminds us of gummatous tissue; but whether similar indura-

FIG. 42.



Syphilitic induration. *a.* Vessels; *bb.* and the other parts left unshaded are bundles of connective tissue which are dissociated by a uniform infiltration with small cells. $\frac{1}{300}$.

tions may not also occur apart from syphilis cannot be decided until we know more about the minute structure of inflammatory indurations in general than we do now.

NOTE.—*Biesiadecki* refers the induration to a certain stiffness and dryness of the fibrous elements of the connective tissue; earlier authors sought it in the quality of the exudation (*Ricord's* plastic lymph, *Michaelis*' exudation flakes—*Exudatschollen*).

§ 111. The syphilitic deposit may also be taken as a type of the lesions caused by LEPROSY and GLANDERS. In these disorders specific tumours are also formed, side by side with simple inflammatory products; the specific tumours continue for long periods in the lowest stage of tissue-development, without undergoing any change; they finally suppurate and burst, or else they undergo fatty degeneration and are absorbed. (For details, *see* chapter on the Morbid Anatomy of the Skin.)

§ 112. TYPHUS. The typhous process is found to differ from simple acute inflammation by the higher degree of development to which the individual cells of the infiltration attain—a degree which brings them nearer to the "epithelial" type. The acme of the typhous changes (with the details of which we shall become acquainted when we investigate the morbid anatomy of the mucous membranes) is known as *medullary infiltration.** If the infiltrated matters are examined, they are found to contain cells differing from simple lymph-corpuscles in containing a greater proportionate amount of protoplasm. The protoplasm of the lymph-corpuscle is barely equal to its nucleus in bulk; while in the cells we are now considering, it occupies at least as much, on an average rather more space than the nucleus. The *typhous cell* represents the lowest stage as it were, the first rudiment of epithelial development; it would seem however that this augmentation of the protoplasm lacks the vigour and permanence of true epithelial development, inasmuch as the typhous cells maintain themselves at this acme but for a short time, and then succumb rapidly to degenerative changes.

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* These observations refer clearly to enteric fever (*Ileotyphus, typhus abdominalis*). I have purposely retained the author's own term, not wishing to define strictly what he has, perhaps not unintentionally, left rather vague. (Cf. § 376).—TR.

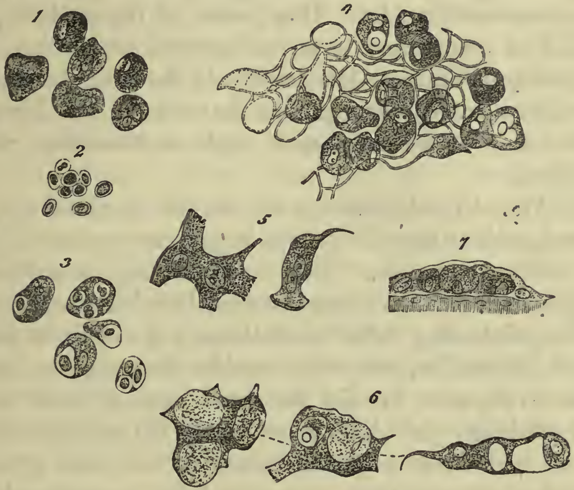
Note.—From a strictly histological point of view the leukhæmic tumour is very nearly allied to the typhous product; the former however cannot be classed among the products of morbid growth without farther evidence. (*See* Chapter I. of Special Part.)

§ 113. Tubercle. A third type of specific inflammation is exemplified by tubercle. I have already pointed out, when speaking of fatty metamorphosis, that the morbid anatomy of the present day does not recognise as tubercle and tuberculisation, what these terms were generally understood to denote little more than ten years ago; viz. every yellowish-white, friable or greasy, in a word, caseous mass, wherever met with. We restrict the term tubercle κατ ’ἐξοχην to a definite nodule, very hard, grey and translucent when first formed, seldom exceeding a millet-seed in size, but aggregated together in great, nay countless numbers. The confusion, both of names and ideas, excited by the rigid distinction first pointed out by *Reinhard*, but carried through by *Virchow*, is not diminished by the circumstance that cheesy inflammation and miliary tuberculosis are very often actually associated with one another. Discoveries of extreme interest have very lately been made on this subject. A series of investigations, started by *Villemain*, carried on by *Klebs* and others, and in some sense concluded by *Cohnheim*, have shown that the introduction of "cheesy *débris*" into the nutrient juices is followed by "miliary tuberculosis." It matters not whether the cheesy matter be introduced by inoculation, or originate in the organism itself. On this view, the minutest particles of cheesy *débris* must be regarded as endowed with the properties of a virus, capable of causing the growth of tubercle by irritating certain (we shall presently see what) elements of tissue. So much is certain, that tuberculosis is the expression of a dyscrasia, of a morbid state of the liquids of the organism, which often spreads through the body from a single point, but which may perhaps in some cases be congenital.

There is hardly an organ in the body in which tubercle is not occasionally met with; but its seats of election are the lungs and intestines. The extensive lesions of an ulcerative character, caused by the growth and especially by the degeneration of the tubercles, will be fully described in the Special Part of this work. I must confine myself at present to what is really the same in all cases, *sc.* the minute structure of the grey miliary nodule, and what we know about its genesis.

§ 114. If we teaze out a miliary tubercle with cataract-needles, we readily succeed in isolating the following elements:

FIG. 43.



Elements shown by teazing out a miliary tubercle. 1. The large tubercle-cells; 2. The small tubercle-cells; 3. Endogenous cell-development; 4. Delicate reticulum from the interior of a miliary tubercle; the cells partly removed by pencilling; 5. Shreds torn from the adventitia of a small cerebral vessel in the neighbourhood of a miliary tubercle. Fission of the nuclei on the inner surface of the adventitia; finely-granular protoplasm accumulated in a continuous layer of considerable thickness; 6. Development of tubercle-cells; 7. The border of a minute vessel, showing the development of tubercle-cells in its adventitia.

1. (Fig. 43)—Large cells, either round, or more often roundly-polygonal, consisting mainly of a finely-granular, highly refracting, seemingly very dense material. The sharp outline, *i.e.* the smooth surface by which the cell is bounded, leads us to assume the existence of a cell-membrane, although this cannot be demonstrated by the appropriate methods (addition of water, crushing, detection of a double contour, &c.). Most of them

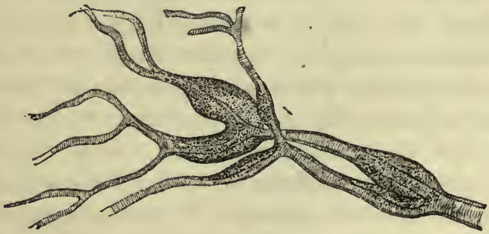
contain a single round nucleus, not of great relative size, very lustrous, usually eccentric in position, though seldom causing any lateral protuberance on the surface of the cell. In some of the cells, we find two, three, or more such nuclei, which undoubtedly originate by fission of the original solitary nucleus; for we also meet with the intermediate stages of the process in the form of elongated, biscuit- (hourglass-) shaped, and even more deeply constricted nuclei. This fission of the nucleus is to be regarded as preparatory to an endogenous production of small cells, utterly unlike those just described; the latter process indeed is not always carried through; so that even in the oldest tubercles, we may occasionally meet with multinuclear giant-cells (*Langhans*).

2. (Fig. 43)—Represents the second form of corpuscular elements, such as may be isolated in greatest number by teazing out a miliary tubercle. They have nothing in common with those just described save their lustrous, dark-bordered nuclei. In all other points they differ from them, and chiefly in their size, which is far smaller, and which enables them during their endogenous development to exist three and more together in one of the parent-cells; they differ moreover by the transparent, homogeneous, and feebly-refracting character of their protoplasm; the exact opposite of these properties being especially characteristic of the larger cells. It is the last-named of these distinctions which enables us to recognise the young cell in the interior of its parent. The appearance of bright areolæ round the nuclei of the latter coincides with the beginnings of endogenous production; we may regard the latter as complete when the bright area is marked off by a sharp line from the surrounding finely-granular and highly-refractive substance of the parent-cell. This phenomenon is illustrated in fig. 43, 3, representing appearances which are very commonly observed.

These cells compose the main bulk of the miliary tubercle. What remains after their removal by pencilling and repeated washing, is the finely fibrous network represented in fig 43, 4, to which we shall have to refer hereafter.

§ 115. Let us now pass on to decide the second question, that concerning the mode of origin and development of the miliary tubercles. We may expect *a priori* to find that this morbid product, like so many others, originates in the conjoint vascular and connective-tissue system. Numerous observations have shown, however, that no connective tissue in the organism is so well adapted for the growth of tubercles, as that which constitutes the adventitia of the capillary arteries and arterioles (Uebergangsgefässe). If *e.g.* we examine a tuberculous pia mater, we may readily convince ourselves that the grey nodules follow by preference the finer ramifications of the arteries. On the larger trunks they adhere, either singly or in little groups, forming one-sided protuberances; on the finer branches, and those vessels which just exceed the capillaries in calibre, they present themselves as spindle-shaped varicosities involving the whole circumference of the vessel (fig. 44). The larger ones exhibit a whitish opacity, beginning at their centre and extending towards the periphery. This opacity is the visible sign of a fatty-granular metamorphosis, of a cheesy transformation, which constitutes the normal mode of degeneration to which the grey granulation is liable. We assume that it begins in the oldest, the first-formed and most central cells; so that the chronological order of the changes which the miliary tubercle undergoes, manifests itself by the formation of concentric zones, the outermost of which consist of the tubercle-cells themselves, while the inner ones are made up of the products of their cheesy metamorphosis. Granting the truth of this assumption, it follows *ex contrario* that we must look for the development of the tubercular elements at the periphery of the nodules.

FIG. 44.



Miliary tubercles on a vessel from the brain.

In the adventitia of the minuter cerebral vessels, a number of very pale, flat, circular nuclei, furnished with nucleoli, are disposed at regular intervals. These may be demonstrated as readily in detached shreds of the membrane, as in those vessels which are still intact. In the latter case, they appear as staff-shaped structures, embedded between the external contour of the vessel and its muscular layer. These nuclei are not naked; they are surrounded by a small quantity of a finely-granular substance, which is chiefly heaped up in the direction of the long axis of the vessel. A second contour, which surrounds the nuclei at a variable distance, may be rendered visible, according to *His*, by the silvering process; this would give the membrane the significance of a lymphatic endothelial tube, though all attempts to arrive at some reliable knowledge concerning its relations to the lymphatic system have hitherto failed. This membrane is the starting-point of the morbid growth, and that too in its capacity as a lymphatic endothelium. The first stage of the process consists in a marked augmentation of the residual protoplasm which surrounds the nuclei. A fissiparous multiplication of the nuclei coincides with it in point of time (fig. 43, 5). The nuclei recede from one another; and while some of them may undergo repeated fission, others enter upon a peculiar change. They assume more of a globular shape in place of their former flattened, discoidal aspect; as a result of this, they become smaller in size; whereas they were pale and finely granular, they now assume a homogeneous lustre; in a word they put on the appearance which has already been referred to as characteristic of the nuclei of the tubercle-cells; at the same time, alterations set in immediately around the nucleus. The protoplasm begins to refract light more highly; its density increases, so that the nucleus looks as if it were surrounded by a spherical envelope of ground glass; the sphere is bounded by a line, indistinct at first, but which subsequently becomes sharper and more definite; this limits the entire structure, and completes the tubercle-cell in all essential respects. Fig. 43, 6, represents shreds of the adventitia torn from the growing border of a small tubercle; in the layer of condensed protoplasm we see on the one hand complete elements with others in process of development, and on the other, cavities which correspond to those elements in form and size; the cells having dropped out during the mounting of the specimen. Fig. 43, 7, shows the edge of a small vessel in whose adventitia several tubercle-cells and nuclei are embedded.

These cells are at first so sparingly produced that wide bridges of protoplasm intervene between them; this also may be seen in fig. 43, 6. As they grow more plentiful, the bridges waste away, the newly developed elements touch each other, and are flattened to some extent by mutual contact. The quantity of residual protoplasm is very trifling. What there is goes to fill that system of inter-communicating lacunæ which is necessarily left between a number of spherical structures when in apposition; it forms a delicate network in whose meshes the tubercle-cells are embedded. Such a network is shown in fig. 43, 4, the cells having been partially removed by pencilling. It consists of fine round threads, which widen out here and there to form small three-cornered expansions. This always denotes that the contact between two adjoining cells has been imperfect, so that a wider film of protoplasm has been left between them. Even nuclei may still be met with in some of the nodal points of the reticulum. The entire structure therefore is in some respects like the finer trabecular networks in the interior of lymphatic glands; and on this ground alone I was formerly led to institute a comparison between the tissue of tubercle and that of the lymphatic glands; and, in common with other anatomists (*Virchow*), to regard tubercle as being actually a lymphoid or lymphomatous morbid growth. What mainly confirmed me in this view however was the similarity between tubercle and the formation of perivascular lymphatic sheaths; the latter process being, in my opinion, the fundamental element in the production of the substance of the lymphatic glands. Meanwhile, however, it was found that the growth of miliary tubercles was inseparably connected, not indeed with the presence of a blood-vessel as such, but only with that of an endothelium. Specific irritation of the endothelia of the lymphatics, the serous membranes, and the blood-vessels (*Schüppel*) is the essential factor in the production of the miliary nodule; and it is only because the lymphatics run by preference in the immediate neighbourhood, in the adventitia of the blood-vessels, that miliary tubercles also exhibit a preference for that locality. (For the development of tubercles on the serous membranes and in the lungs, *see* special chapters on the morbid anatomy of those organs.)

4. Histioid Tumours.

§ 116. On the capacity of the intermediate apparatus of nutrition for generating embryonic tissue at nearly any point in the body, are also based those higher products of tissue-genesis which we term "growths" in the strictest sense of the word, or more correctly *histioid tumours.* These are characterised by the internal continuity of their constituent elements. The majority are made up of only a single tissue; should they be composed however, of more tissues than one, the component tissues are never isolated, never marked off, as epithelium is marked off from connective tissue, but are in organic continuity with one another. The explanation of this internal continuity is to be sought in the original unity (Gleichartigkeit) of the material of which the tumour is built up, this material being in every case embryonic tissue. From this, by a subsequent process of differentiation, are developed tissues of a higher type, more particularly the connective substances—connective tissue proper, with those of its varieties which occur in inflammatory products (Fibroma and Sarcoma), cartilage (Chondroma), bone tissue (Osteoma), adipose tissue (Lipoma), mucous tissue (Myxoma); the higher anomalous tissues, such as the muscular (Myoma) and the nervous (true Neuroma) are more rarely produced. Their mode of origin however is precisely the same as in fœtal development; *i.e.* a certain number of embryonic cells are converted into the specific elements of cartilage, bone, fat, or muscular tissue, while the remainder go to form connective tissue; moreover, an adequate vascularisation partitions out the resulting structures into territories of nutrition, thus incorporating them with the organism as a whole. This ensures the interdependence of the tissues among themselves, as well as their connexion with the organism; the morbid product taking its place as an organ, though a malformed and unnecessary one. Growths of colossal size are often produced without in any way affecting the integrity of the body; such growths only requiring removal by the knife to reestablish the *status quo ante.*

§ 117. This last statement requires some qualification. Unfortunately there exist, even among histioid tumours, a certain number to which we are compelled to ascribe a "malignant" character (Malignitas).

We call a tumour "malignant," not merely because it endangers the life of its host, but because it threatens his life in one particular way, by exciting a definite constitutional malady which is incompatible with the due continuance of the general nutrition of the organism. The symptoms of this general malady (*Cachexia*) are: prostration of strength, diminution in the amount of blood, watery blood, emaciation, earthy tint of skin, profuse sweating, diarrhœa, hæmorrhages, &c., to which the patient finally succumbs.

All attempts to detect the cause of this general disease by chemical or microscopical investigation have hitherto proved unsuccessful. How the malignant tumour gives rise to the cachexia is still unsettled. Those who regard the tumour as primarily a local disease are very naturally interested in identifying the marasmus in question (which is always secondary) with the constitutional tumour-dyscrasia (Geschwulstkrankheit) of the humoral pathologists, and in deriving both equally from the infecting action of the malignant growth. This view has especial claims upon our favour; for one thing at least remains beyond all question, viz. that a stimulus is propagated from the primary growth which excites the development of similar deposits elsewhere, and which gradually extends its influence over the entire organism. In this extension of the formative stimulus, the so-called "constitutional infection," we recognise three distinct stages.

§ 118. During the first stage its operation is confined to the immediate neighbourhood of the primary tumour. It determines the continued production of new foci at the periphery of the central growth, with which they subsequently coalesce. Malignant tumours therefore invariably extend by peripheric infiltration (§ 69, 3). We are obliged to assume that the impulse to morbid growth precedes the growth itself by a certain interval of time. This we learn from what is known as the tendency of malignant tumours to recur after extirpation. Suppose we remove the entire tumour, together with its zone of peripheric infiltration, with a view to arrest the mischief. The incision appeared after the operation to have been wholly within the limits of the healthy tissue; nowhere could we detect even a trace of pathological proliferation. Nevertheless, in the majority of cases we find, to our dismay, that a fresh tumour, similar in character to the one removed, recurs at the seat of operation, from the very tissues which seemed at the time so entirely healthy. Unless therefore we adopt the theory of a dyscrasia, we are driven to assume that the tissues, even when already affected by the formative stimulus, afford no visible signs of this till after a certain time has elapsed.

§ 119. The second stage is characterised by the implication of those lymphatic glands which receive the lymph from the region primarily affected. There can be no doubt that some material stimulus is conveyed by the lymphatics. But what is it? We might think of cells. We know that even coarser particles, *e.g.* insoluble pigments, rubbed into the abraded cutis in tattooing, are taken up by the lymphatics, and carried to the nearest lymphatic glands, where they are deposited. But may we conscientiously resort to this analogy? After recent injuries the lymphatics gape, and are well able to take up material particles. Are we justified even in suspecting the existence of some such condition of the lymphatics in the neighbourhood of a tumour? The pigment-granules are either heavy, sharp, or hard particles, which, in consequence of any one of these qualities, and aided by friction of the tattooed surface, are able to penetrate in any direction through the soft parenchyma of the body as far as the lymph-canals. We cannot say the same of cells. *This* analogy therefore must be put aside; but its rejection does not necessarily involve the rejection of the hypothesis that the lymphatic glands are infected by the transport of cells. On the contrary, thanks to the discovery that young cells are enabled by their amœboid contractility to penetrate through the connective tissue in all directions, we are no longer at the mercy of the analogy above alluded to; with a degree of probability verging on certainty we can assign the infection of the lymphatic glands, and of the entire body, to the tumour-elements themselves, or to such young cells as have acquired infecting powers by direct contact with them.

The implication of the lymphatic glands is held to be a proof of the infecting power of a tumour, and so far as of unfavourable augury. This outweighs the more sanguine theory (which has been started more than once), that the zymotic virus is shut out from the rest of the organism by closure of the lymph-paths in the interior of the swollen glands. When we come to study the details of this sort of "closure by swelling," we shall find it necessary to admit that it may very probably *retard* the progress of infection. The delay, however, is never more than temporary; it never amounts to an arrest of the process.

§ 120. The third and last period in the propagation of the tumour shows us that even the sacrifice of several lymphatic glands has not preserved the organism from constitutional disease. The production of secondary deposits in other regions of the body is known as *metastasis.* Whether this designation is justified by the actual transfer of material particles from the seat of primary mischief and the diseased glands to more remote parts, is open to all the doubts previously expressed; the most active investigation has hitherto failed to demonstrate the tumour-elements in the blood, through which their transit must inevitably take place; so that here also, prudence bids us confine ourselves for the time being to the hypothesis of some zymotic material existing in the blood.

Whoever rejects the theory of a dyscrasia, sees in this radiation of the formative stimulus from the seat of primary disease a summary presentment of the relation in which every malignant growth stands towards the organism. He who supports the doctrine of a primary constitutional disorder occupies a far more difficult position. He may insist however: 1st, that the cachexia cannot as yet be fairly identified with the constitutional infection, and 2nd, that the formative stimulus must be the same for the primary tumour as for the secondary deposits; and that the difficulties in the way of explaining the origin of the primary tumour, save on the hypothesis of an antecedent dyscrasia, remain as great as they ever were. For my own part, I do not feel called upon to anticipate in any way the coming solution of this problem.

§ 121. Having agreed upon the clinical significance of malignity, we may proceed to inquire, whether there are any anatomical signs by which malignant tumours may be recognised, before their malignity is proved by the occurrence of metastasis; to this inquiry, we return the same answer as *Waldeyer*, namely, that tumours tend as a rule to become generalised in direct proportion to the vascularity of the soil in which they grow, and to the number of mobile cells present in their interior, or immediately around them. We still have plenty to do in trying to increase the store of our experience concerning this most important subject, by the thorough histological investigation of every tumour which comes under our notice, combined with a careful record of the farther progress of each case. For the present, we will content ourselves with stating the degree of malignity of each individual species of tumour, so far as the experience at our disposal will allow. It will be seen that "cancerous" growths stand foremost in order of malignity, but that some of the histioid tumours (viz. sarcomata and enchondromata) are also endowed with a certain measure of malignity, which is not always assignable to their being combined with cancer.

§ 122. Before dismissing this important subject, several points nearly allied to malignity, but which ought not to be confounded with it, must be placed in their right light. First among these is the general question of danger to life. A tumour may, by its position, its size, its weight, &c., not only occasion the greatest inconvenience to its host, but may be the direct cause of his death without being entitled, on this ground alone, to be called malignant. A fibroid growth in the prostate obstructs the urethra and causes death by retention of urine; a fibroid of the uterus endangers life by hæmorrhage; we are not justified on such grounds in terming either of these tumours malignant. Neither can the multiple character of a tumour be regarded as *ipso facto* evidence of its malignity. When we find sarcomatous growths in various parts of the skeleton; when eruptive foci co-exist on the calvarium, the tibiæ, the clavicle and the vertebral column, we may legitimately infer that the entire osseous system is diseased, and we may suspect a general disease of bone, analogous to the general affection of the skin in the exanthemata; but it would be a mistake to try to identify this primary generalisation of the growth with that secondary generalisation which is peculiar to malignant tumours. The two are independent of each other.

a. *Sarcomata.*

§ 123. On comparing any sarcoma, as regards its colour and consistency, with muscular tissue, we find it hard to understand how these tumours can ever have received the name of "flesh-tumours" (sarcoma from σάρξ). It is true that in common parlance many things besides muscle are called flesh; for instance, granulations are commonly spoken of as "fleshy," and if the name "sarcoma" were derived from this application of the term, the comparison might be regarded as a very apt one, and that on more grounds than one. For the sarcomata are the most interesting of all histioid tumours, just because they undoubtedly repeat that group of tissues with which we became acquainted among the heteroplastic products of inflammation. We meet once more with the round-celled embryonic tissue of granulations, and with its lymphadenoid variety (*caro luxurians*), with spindle-cell tissue, and the densely fibrous connective tissue of cicatrices. As a rule, we find several of these tissues in combination—combined however in such a way, that one of them constitutes the main bulk of the growth, while the others are present in smaller proportions. The tumour is named after its chief constituent, *a potiori fit denominatio*. Accordingly, we distinguish three main categories of sarcomata, *sc.* round-cell sarcomata, spindle-cell sarcomata, and fibromata.

The secondary constituents are never co-ordinate with the principal tissue; they are either preliminary stages in its development, or products of its farther metamorphosis. These metamorphoses occur in the same order as in formative inflammation; the round-celled tissue (granulation-tissue) stands first in point of time; it is converted into spindle-cell tissue, which in its turn gives rise to fibrous tissue. We must not however shut our eyes to the fact that the series of possible evolutional forms is not restricted to the histological products of formative inflammation. Cartilage, bone, mucous and adipose tissue are met with in sarcomata as results of their secondary metamorphosis. Of course they occur only as subordinate constituents, and enable us to establish varieties; the tumours in which they predominate, or in which they exist alone, forming the farther classes of the heteroplastic histioid growths, the myxomata, lipomata, enchondromata and osteomata. This shows us the close inter-connexion of all histioid tumours and helps us to unite them into a single group.

The origin and growth of sarcomata vary for each species;

we may affirm generally that growth by infiltration of surrounding tissues, the so-called peripheric mode of growth, occupies a subordinate position; central growth, increase by internal apposition, taking the first place. The fibromata afford exquisite examples of central growth; the medullary round-cell sarcomata incline rather to the peripheric mode of increase; the spindle-cell sarcomata, in this as in other respects (*sc.* as regards malignity) occupying an intermediate position.

It would be possible to constitute a long series of species and sub-species of sarcomata, were all those modifications to be taken into account which are mainly due to the seat of the tumour. I prefer to confine my remarks to a limited number of typically recurring forms, and to relegate the consideration of the special sarcomata of individual organs and systems to the second part of this treatise. Among such special forms I place the ossifying sarcoma of the periosteum and the giant-cell sarcoma of the medulla of bone, the glioma of the central nervous organs, the cystosarcomata of the various glands, &c. I will also avoid all reference at present to the finer shades of difference between the leading forms; in my own experience, there is hardly any tumour which has not some shade of difference peculiar to itself; nay, I would go so far as to assert, that tumours *exactly* similar to one another can only occur at *exactly* the same point in the organism.

ROUND-CELL SARCOMATA.

§ 124. I.—*The granulation-like round-cell sarcoma* (sarcoma globo-cellulare simplex). In texture and composition this form of sarcoma approximates most nearly to the type of granulation-tissue. It presents itself to the naked eye as a yellowish or reddish mass, homogeneous throughout, soft yet elastic, and occasionally very like fish-roe; from its cut surface a scanty juice may be scraped; this juice is nearly clear, or else contains but a small proportion of cells. The cells are small in size, round, and contain relatively large, sharply-defined nuclei, furnished with nucleoli. As a rule, there is but little protoplasm, and what little there is is quite naked; to make it visible, and to convince ourselves that each of the seemingly free nuclei is really part of a cell, we are obliged to have recourse to hardening the tumour and staining it with carmine.*

The structure of a round-cell sarcoma differs from that of ordinary granulations only in degree. Some of the vessels are wider and have thicker walls; but where they break up into capillaries, they are quite as frail as those of granulation-tissue, consisting frequently of no more than a single layer of cells. Their interstices are uniformly packed with the round-cells, and the scanty, soft, amorphous matrix of the embryonic tissue. In rare cases, the entire tumour is more highly differentiated; it recalls the papillose variety of granulations, exhibiting radiating striæ, along which it has a tendency to split up. On a subsequent opportunity we will say more about these fasciculated round-cell sarcomata which spring by preference from the periosteum, where they are known under the name of *sarcoma ossificum.*

The simple round-cell sarcomata originate most commonly from membranous expansions of connective tissue; they grow by preference from the periosteum and the membranous investments of the nervous centres; we must however be prepared occasionally to recognise them in other parts as well, in the skin, the mucous and serous membranes, nay even in the glands. The simple round-cell sarcoma is closely related to the small-celled spindle-cell sarcoma, and through this to the fibroma; it often passes continuously into these forms. In harmony with this is the comparative benignity which distinguishes this variety among all other round-cell sarcomata.

§ 125. II.—*The lymphadenoid round-cell sarcoma* (sarcoma lymphadenoides, molle). This variety owes its softer texture mainly to the circumstance that its cellular elements are less closely aggregated than those of ordinary granulation-tissue. On scraping its cut surface a juice, loaded with cells, is readily obtained; on microscopical examination these prove to be round-cells with large, oval nuclei, which refract light but feebly, and are each provided with a point-like nucleolus. On hardening the tumour and pencilling out a fine section, we discover a delicate intercellular network, which forcibly reminds us of the reticulum of the lymphatic follicles, the alimentary mucous membrane, and the *caro luxurians* (fig. 45). This network is stretched between the wide, thin-walled capillaries, and imparts a certain consistency to the entire structure, while permitting fluid to collect in abundance round the cells, and thus favouring their isolation.

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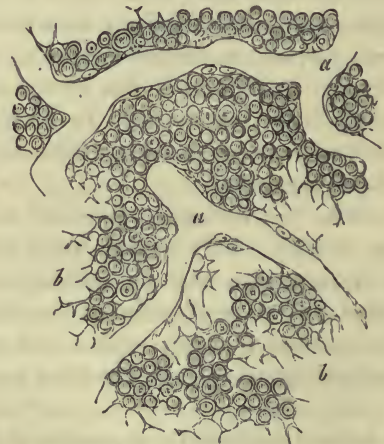
* *Virchow* is inclined to ascribe the appearance of the seemingly free nuclei to an excessive frailty of the bodies of the cells; and he takes the opportunity of adding an observation which all practical histologists should lay to heart (On Tumours, p. 204); "this frailty of the cells is so striking, that I have long been in the habit, whenever a recent tumour seems to consist mainly of large, naked nuclei, with large, lustrous nucleoli, of at once suspecting that I have to do with a sarcoma."

This form of sarcoma originates most frequently from the subcutaneous, subfascial, and intermuscular connective tissue of the thigh. Next in order of frequency come the lymphatic glands. In this case however we are met by the singular difficulty that the anatomist may be misled by similarity of structure into regarding the sarcoma as a simple overgrowth, however monstrous, of the glands; while its clinical mark (one of extreme malignity) indicates its absolute identity with the soft variety of sarcoma. (*See* Lymphatic Glands.)

FIG. 45.



Round-cell sarcoma. *a.* Lumina of vessels; *b.* Parenchyma partially pencilled out to show the delicate network formed by the hardened matrix. $\frac{1}{300}$.

There are several varieties of the lymphadenoid sarcoma. The *lipomatous* variety (sarcoma lipomatodes) is characterised by having its cells partially converted by fatty infiltration into fat-cells. This transformation is always restricted to a limited number of the elements present; inasmuch however as the altered cells arrest attention by their lustre and their size, it may very readily seem as though the vast majority, if not all, of the sarcoma-cells had been converted into fat-cells. The resemblance to genuine adipose tissue does not go very far; the lack of uniformity in the infiltration, and the promiscuous assemblage of very large and very small fat-cells, which are never united into clusters, make it impossible to confound these tumours with lipomata.

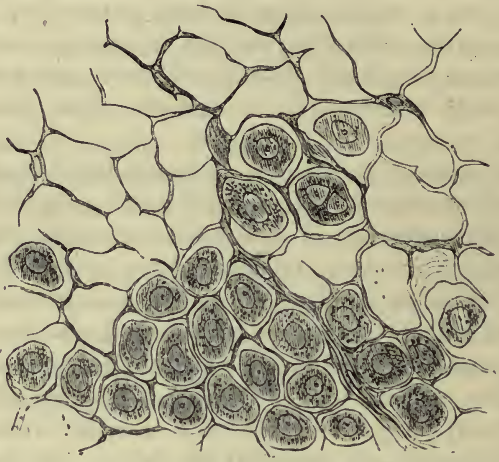
The *myxomatous sarcoma* (s. myxomatodes). Small portions of mucous tissue are not unfrequently found embedded here and there in the substance of round-cell sarcomata. Such islets betray themselves even to the unaided eye by their transparent, jelly-like, tremulous consistency; the microscope usually demonstrates an abundant proportion of mucous basis-substance, with a great number of round-cells which do not anastomose with one another, embedded in it. Mucous softening of the basis-substance may justly be regarded as a secondary metamorphosis to which all round-cell sarcomata are liable. The possibility of this change occurring at an early period in their development, and its extension through large portions of a tumour, justifies the term "myxomatous sarcoma." Nay, the mucous tissue may so exceed the proper structure of the tumour in amount, that we might be led to think of a true myxoma, but for the presence of some few unaltered portions; these, and more particularly the youngest products at the periphery of the tumour, and its striking metastases, place its sarcomatous nature beyond the possibility of question. The extremely rapid rate of growth which is characteristic of myxomatous sarcomata might be inferred from the fact that mucus, owing to its capacity for swelling by imbibition, takes up a volume disproportionately greater than that occupied by the scanty intercellular substance of the sarcoma.

Mucous metamorphosis and fatty infiltration often co-exist; such tumours are peculiarly prone to assume a colossal size.

The lax connective tissue of the extremities and the subperitoneal connective tissue are the seats of election of the mucous variety of sarcoma.

The *large-celled round-cell sarcoma* is distinguished by the approximation of its cells to the epithelial type, and by an intercellular network with meshes of proportionate size (fig. 46). This tumour is very soft, cerebriform, and therefore easily confounded with the next species.

FIG. 46.

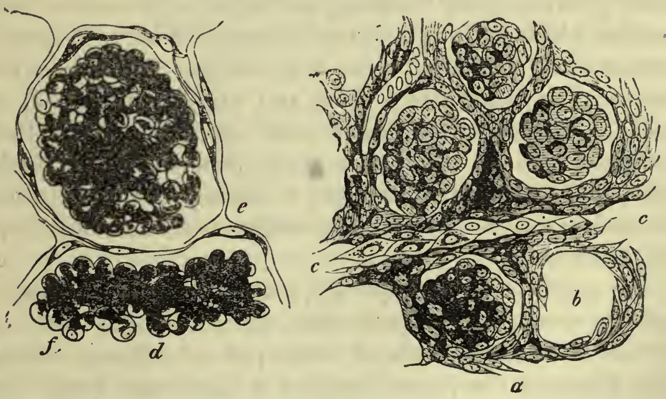


The large-celled round-cell sarcoma. $\frac{1}{300}$. (After *Billroth*).

III.—*The alveolar round-cell sarcoma* (*Billroth*) (sarcoma medullare, carcinomatodes) represents a farther advance in the independent evolution of the cells, analogous on the one hand to the suppuration of an inflamed texture, while on the other it recalls that more sharply-defined contrast between the connective tissue and the corpuscular structures which we shall find in cancer. Characteristic of this variety is the occurrence of globular masses of cells, which are no longer held together by any proper matrix, but resemble the pus-corpuscles of a minute abscess in occupying a gap of appropriate size in the continuity of the connective tissue. This must not be taken to imply that the cells in any way resemble pus-corpuscles; on the contrary, they are notably larger in size, they are provided with round, vesicular nuclei containing lustrous nucleoli, and verge far more nearly on the epithelial type, which in solitary instances they may even simulate in the most deceptive way. And here I go farther than many will be disposed to follow me; I regard the structure in question as being really a cancerous degeneration of the sarcoma (s. carcinomatodes). In my opinion, we are no longer justified in regarding that cancerous type of structure which is co-extensive with the clinical denotation of carcinoma, as based exclusively upon the primordial opposition between connective tissue and epithelium. "Stroma" and "embedded cells" may be produced in more ways than one, and "epithelioid" is not synonymous with "epithelial"; though we may feel puzzled to explain how it is that those cells which separate from the parent soil in a more *organic* manner, slowly, and not suddenly like the corpuscular elements of pus, should invariably exhibit this tendency towards a more epithelial type of development. For there is just this distinction between genuine suppuration and this simulacrum of it, that we cannot simply regard the globular aggregations of cells as being wholly *outside of* the nutrition of the body. Their continued existence without undergoing fatty degeneration affords sufficient proof of this.

S. carcinomatodes occurs in the most diverse parts of the intermediate apparatus of nutrition; it is most frequent in the marrow of bone, in the eye, in the subcutaneous tissue. A peculiarly malignant variety, characterised by the pigmentation of its cells, is known as *pigmentary cancer* (s. alveolare pigmen-

FIG. 47.



Alveolar round-cell sarcoma, pigmented. *b*. An alveolus from which its proper globe of round-cells has dropped out; *c*. Vessel, with pigmented endothelia; *d*. Pigmented round-cells; *e*. Spindle-cells, forming stroma.

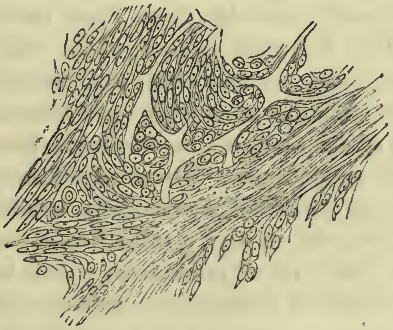
tatum). The provisional diagnosis of this variety is based on the great softness and dark colour of the tumour. On microscopical examination we find, side by side with the alveolar structure in which its growth culminates (fig. 47), parts of variable size, illustrating earlier stages in its development. Most common is an infiltration of the connective tissue with pigmented round-cells; the transition from this to the medullary structure being operated by circumscribed aggregations of such cells. In other cases a well-marked sarcomatous texture, oftener of the spindle-cell than of the round-cell kind, has obviously existed alone for a considerable time before the characteristic globes of cells can have been developed. This leads us to believe that the melanoses generally are very closely related to one another; a view which will be more amply developed when we come to speak of what is vulgarly known as "pigmentary," or "melanotic" sarcoma.

SPINDLE-CELL SARCOMATA.

§ 126. IV. *The small-celled spindle-cell sarcoma* (s. fuso-cellulare durum) stands in the same relation to other spindle-cell sarcomata as the granulation-like sarcoma towards the remaining round-cell sarcomata. It deviates least from the type of inflammatory growth, closely imitating that spindle-cell tissue of recent cicatrices which constitutes the permanent link between granulation-tissue and the fibroid tissue of cicatrices. The characteristic element of its texture is a short and narrow spindle-cell, containing a roundly-oval nucleus with or without a nucleolus. The protoplasm of the cell is finely-granular; it is thickest immediately around the nucleus; a limitary membrane cannot be certainly shown to exist; the smaller cells are undoubtedly devoid of one.

The spindle-cells of which the tumour is made up are very regularly dovetailed into each other, the acute angle left vacant between the pointed ends of every pair of adjacent elements being filled by the pointed end of a third one, lying either behind or in front of them. No trace of any interstitial substance is to be detected; in no case is there more of it present than there is in granulation-tissue; but this minimum, which is really nothing more than an amorphous and glutinous cement to keep the cells together, cannot be supposed to be lacking even in spindle-cell tissue; by its aid, and owing also to the harmonious coaptation alluded to above, bands of cells are formed, bundles of variable thickness, which constitute the proximate structural elements of the spindle-cell sarcoma. The bundles very rarely radiate from a single centre; more commonly we find a number of centres; the various systems of fasciculi being interwoven with one another in the various lines indicated by the position of those points. As a general rule however, we are not able to detect any definite plan in accordance with which the bundles are combined to form a single whole. In every section we examine (fig. 48) we find some fasciculi divided longitudinally, others transversely, others again in a more or less oblique direction. An attempt has been made to connect the course of the cellular bands with that of vessels; but this is altogether wrong; for although the thicker fasciculi invariably contain an axial vessel of considerable size, this is true of the thicker fasciculi only. With this exception, the vessels form networks, just as in other parenchymatous structures, permeating the cellular bands in all directions. Moreover all the vessels of a sarcoma, including those of larger calibre, have as good as no proper walls; they present themselves in transverse sections of hardened specimens as simple canals, tunnelled and drilled through the tissue.

FIG. 48.

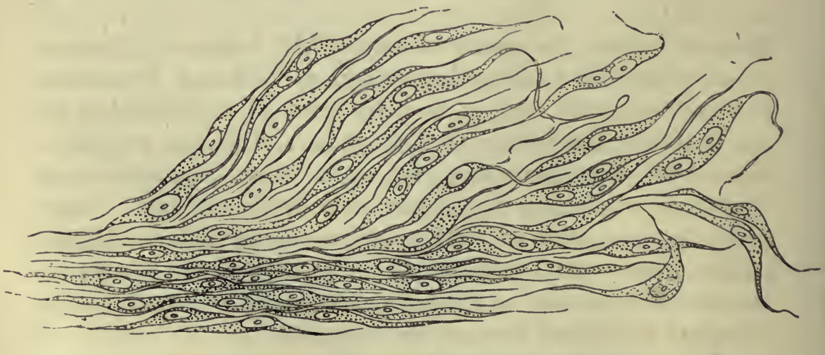


Spindle-cell sarcoma. Vessels gaping. The cellular bands divided, some transversely, some longitudinally. $\frac{1}{300}$.

The small-celled spindle-cell sarcoma grows by preference from fibrous membranes, fasciæ, sheaths of vessels and nerves, the subcutaneous and submucous connective tissues; in a word, its seats of election are the same as those of fibroma; indeed, the two not unfrequently occur together (*e.g.* in the uterus). Moreover, in all such sarcomata there are parts where the spindle-cell tissue passes into fibrous connective tissue; tumours occur, which are made up of both these tissues in equal proportions; so that the connexion between this variety of sarcoma and fibroma is so intimate as almost to amount to identity.

V. *The large-celled spindle-cell sarcoma* is much more than a mere variety of the preceding form. It differs from it in one most important point; the disproportionate development of its cells as compared with all the remaining elements of its structure. The spindle-cells may attain the very considerable thickness of ·015‴, and a length so enormous, that their two extremities, under a magnifying power of 200 diameters, are separated from each other by three times the diameter of the microscopic field. The thickest part of the cell corresponds in position to the large, roundly-oval nucleus, with its lustrous nucleolus. The protoplasm is finely-granular and soft in the neighbourhood of the nucleus; as we recede from the nucleus it becomes more homogeneous. No cell-membrane can be shown to exist; but the processes occasionally exhibit so marked a degree of tenacity, and so high a refractive power, that we must regard them as made up of protoplasm which has grown rigid. The name "spindle-cell" implies the existence of two such pro-

Fig. 49.



Large-celled spindle-cell sarcoma, after *Virchow.*

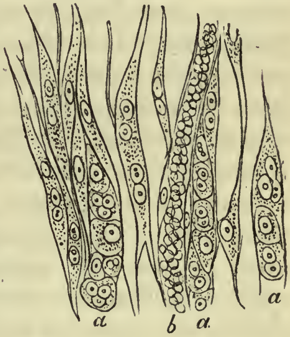
cesses; exceptionally however, we find three or more, giving the cell a stellate character (*Virchow*).

In typical examples of spindle-cell sarcomata the cells unite to form bands of considerable size, leaflets, and fasciculi. These may radiate in straight lines in every direction from a common base (radiating sarcoma, foliated sarcoma); or they may be elaborately interwoven with one another (trabecular sarcoma). These tumours may grow to a very considerable size without undergoing any farther modification of structure or composition. The enormous growth of the cells is in some measure vicarious for the due production of fibrous intercellular substance; and if we are disposed to agree with *Max Schultze* in viewing the latter as simply metamorphosed protoplasm, this would be a case in which building materials had been generated in profusion, but not used.

The large-celled spindle-cell sarcomata start from fasciæ and membranes, seldom from the interstitial tissue of glandular organs. Their malignity is restricted in degree; they very seldom recur after timely extirpation. Of course they must be carefully distinguished from cancers and medullary sarcomata with a radial structure.

The only variety of the large-celled spindle-cell sarcoma is a tumour which is met with in the skin of the cheek; it is essentially a combination of the round-cell with the spindle-cell type. Broad, fibrous bands of spindle-shaped cells diverge from one or more centres; the intervals between them are occupied by the round-cell tissue. This arrangement is represented in fig. 50. We see the colossal spindle-cells, with their long bodies and yet longer processes, enclosing long meshes in which the round-cells are embedded.

FIG. 50.



Large-celled sarcoma. A place in which parallel rows of colossal spindle-cells are mingled with round-cells. *a*. Round-cells; *b*. Vessel. $\frac{1}{300}$.

VI. *The pigmentary* or *melanotic sarcoma* (s. melanodes), starts most commonly from the choroid coat of the eye; next in order of frequency from the skin; both parts, in which the cellular elements are normally infiltrated with a certain amount of pigmentary matter. Pigmentation is usually explained by supposing that the morbid growth inherits the vital peculiarities of those cells from which it sprang. But this doctrine must not be too rashly accepted. The metastatic deposits, which, owing to the well-marked malignity of the melanotic sarcoma, are by no means rare, exhibit the same disposition to pigmentary infiltration, though developed in parts where no physiological pigmentation is known to occur. This transfer of a purely local peculiarity to the secondary tumours has been advanced both for and against the doctrine in question. For it, by those who hold that metastasis is caused by the transfer of material elements from the primary tumour to other parts; against it, by the believers in a constitutional dyscrasia which generates black tumours, where it generates any tumours at all.

We ought, in my opinion, to distinguish as clearly as we can between the two following points: 1st, the exciting of the metastatic deposit by cells which have migrated from the primary tumour; and 2nd, the pigmentation of the secondary tumour. With regard to the former, I refer the reader to the hypotheses and scruples enunciated in § 120; with reference to the latter, it must be understood that all the cells of a melanotic growth are originally colourless. No one will assert that they are directly descended from cells which have migrated from the primary tumour; on the contrary, their local origin is beyond all question; and as they nevertheless become pigmented, we must needs ascribe their pigmentation to a constitutional tendency which is independent of the seat of origin of the primary tumour. Etiological experience accords with this view; it teaches us that an over-production of pigment is, at all events in the skin, a predisposing element in the causation of these tumours. This over-production manifests itself either in the growth of black warts which may degenerate directly into melanotic sarcomata, or in a black or brown staining of the skin, whether diffuse or circumscribed. The special predisposition of creatures totally devoid of pigment, *e.g.* of white horses, to become affected by melanotic sarcoma, may be explained on the theory of a vicarious pigmentation, the deposit occurring at a single point, and being therefore associated with a certain degree of tissue irritation.

In all melanotic tumours the cells are the exclusive depositaries of the pigment. The histological details of pigmentary infiltration have been fully described in the early part of this work; the reader may refer to the corresponding sections. I there repudiated, as regards melanotic growths, the hypothesis which derives pigmentation solely from antecedent hæmorrhages, substituting the view that in such cases soluble blood-pigment was taken up from the blood. I arrived at this conclusion, apart from the lack of evidence in support of the hæmorrhagic theory, from considering how pigment first originates in tumours which have existed for a considerable time as simple medullary sarcomata, and have subsequently become melanotic; recurring as such after extirpation and giving rise to secondary deposits of the same kind. In such tumours we are often able to determine that the earliest traces of pigmentary infiltration appear in *the epithelial cells lining the vessels.* Can this be explained otherwise than by supposing that the epithelial cells take up the diffused colouring-matter from the blood? that it becomes concentrated and then precipitated in a granular form in their interior? And when pigmentation of precisely the same kind makes its appearance at a later period outside the vessels, and finally extends throughout the entire parenchyma of the tumour, I cannot see any reason for doubting that here too the phenomenon takes place in the same manner as in the epithelial cells which line the vessels—by the absorption of diffused colouring-matter from the blood.

§ 127. In comparison with the general pathological relations of melanotic tumours which have just been discussed, their position in the anatomical scale is a question of subordinate moment. What is vulgarly known as melanotic cancer has already been described (§ 125) under the name of alveolar round-cell sarcoma, or medullary melanotic sarcoma. The remaining melanotic growths belong for the most part to the group of spindle-cell sarcomata. Their consistency is generally firmer; their texture fasciculated or foliaceous. Their well-marked tendency to project above the surface, to form tuberous and fungous elevations, a tendency which they have in common with the round-cell sarcomata, distinguishes them very notably from the destructive carcinomata. As regards their colour, we must bear in mind the principle above referred to (of the colourless condition of their elements when young), as a standard of comparison. Melanotic sarcomata of great size occur, which betray their true character at first only by a black or brown marbling, a mottled or piebald appearance. The deep brown-black, sepia tint is confined to the most extreme degree of pigmentary infiltration.

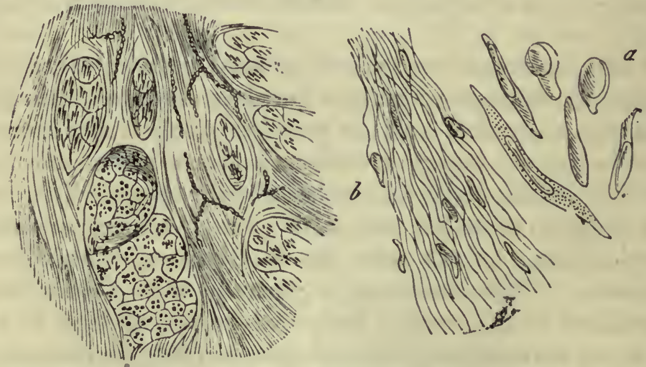
A fibromatous character is only exhibited, according to *Virchow*, by the melanotic fungosities of white horses, alluded to above; tumours differing in their benign character from all other melano-sarcomata, which are invariably malignant.

Fibrous Sarcomata.

§ 128. VII. *The Fibroid.* I cannot separate the fibromata from the sarcomata. Just as we sought the prototypes of the round-cell and spindle-cell sarcomata in the round and spindle-cell tissues of inflammatory proliferation, so we shall find the prototype of the fibromata in the formed tissue of cicatrices.

The common fibroid (desmoid) consists of a fibrous, reddish-white, stiffly-elastic substance, so dense and tough or even hard, that it creaks under the knife. Its structural elements are identical with those of cicatricial tissue. If we tear off a fine fibril from the cut surface of the tumour, and tease it out, we are amazed at the enormous bulk which it assumes, *i.e.* at the enormous number of yet finer fibrillæ into which it allows itself to be broken up. The microscope shows us, moreover, that each

Fig. 51.



Transverse section through a fibroma of the uterus. $\frac{1}{300}$. *a.* Isolated cellular elements; *b.* fasciculus teased out to show its component fibrillæ. $\frac{1}{500}$.

of these finer fibrillæ is itself made up of other fibrillæ of extreme tenuity, apparent to the eye as mere lines, though sharp and definite lines (fig. 51*b*). Just as a well-plaited braid takes up infinitely less space than a tress of unkempt hair, even though the number of hairs may be the same in both, so we may suppose that in the fibroma the fine and finest fibrillæ are very closely packed, taking up an amazing amount of space when separated by our needles.

Between the fibrillæ, which are composed of a gelatigenous material, and represent a fibrous intercellular substance, we can see the cells (fig. 51*b*). These are usually small, roundly-oval, and furnished with lustrous nuclei. In fig. 51*a*, I have figured these elements under a high power, mainly because *Virchow* has been led, by their great resemblance to the fibre-cells of unstriped muscle, to set up a "fibro-muscular tumour" as a special variety of fibroma. I do not wish for a moment to question this resemblance; it would be very difficult to draw a hard and fast line between spindle-cells and unstriped muscular fibres so far as their minute structure is concerned; meanwhile I think it desirable to begin by comparing sarcoma with inflammatory proliferation, the spindle-cells of the tumour with those of the cicatrix. This furnishes us with a practicable basis for understanding all the structural elements which are met with in the fibroid.

It is only the chief constituents of the tumour that have been hitherto described; besides these we find: 1st, bands of spindle-shaped cells which traverse the tumour in all directions; 2nd, rounded deposits of embryonic tissue which lie embedded here and there in the continuity of the fibrous bundles. I regard both of the above as transitional structures from which the fibrous tissue is developed in just the same way as the cicatrix is developed from the embryonic and spindle-cell tissues. In a single uterus, I found a number of fibromata, the larger ones consisting mainly of fibrous tissue, while the smaller ones were almost entirely made up of spindle-cell tissue.

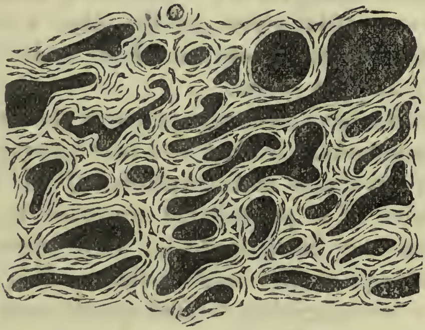
The appearance of the tumours on section deserves especial notice. The tortuous and interlacing bundles of fibres give it a most peculiar aspect. Microscopic examination (fig. 51) analyses the naked-eye appearances into their details, without shedding any light on the cause of this arrangement. In some cases, the concentration of the morbid growth around the vessels and nerves of a part appears to exert some influence on its internal arrangement. For instance, *Billroth* has described a fibroid tumour of the eyelids (which he afterwards sent to me for examination), consisting of a number of sausage-like cylinders, in whose axes the remains of minute nerve-trunks were distinctly traceable. Treading in his footsteps, *Czerny* has recently separated a group of sarcomata, under the name of "plexiform tumours," adding the announcement that the branches of the vessels might occasionally serve as well as those of the nerves to determine the singular composition of the growth. The most striking case however, is when all the vessels of a primarily myxomatous tumour are surrounded by comparatively thick sheaths, which consist throughout of round-cells. In the ordinary variety of fibroma, the course of the vessels does not seem in any way related to that of the fibrous bundles. It appears to me far more likely that as the fibroma (which is an exquisite example of the central mode of growth) increases in size, the newly-formed products are intercalated between the existing fibrous bands, which are thereby dissociated; and that the incompletely laminated structure of the growth is thus accounted for by a repeated process of interstitial dissociation, and not by concentric addition of the newly-formed products.

Fibromata are justly counted among the most benign of all morbid growths. We shall find hereafter that the uterus is their favourite seat; and we shall then become acquainted with a series of interesting modifications of the structural type which has been just described.

§ 129. VIII.—*The cavernous tumour.* The tissue of the corpora cavernosa penis, with whose structure the reader is supposed to be familiar, is the physiological prototype of the cavernous tumour. We find the same network of white, glistening trabeculæ of connective tissue, in whose wide meshes (wide enough to be seen by the unaided eye) the blood is contained as in a sponge (fig. 52); we find the same elasticity of the trabecular network, which allows of periodical variations in the amount of the contained blood, causing alternate swelling and subsidence of the growth; finally, I have convinced myself by a series of observations specially directed to this point, that the mode of origin of the spongy or erectile tissue is the same in both cases.

I call the way in which the cavernous tumour is produced, a "cavernous metamorphosis." For I have arrived at the conclusion, which might have been anticipated *a priori*, that every vascular tissue is susceptible of undergoing conversion into erectile tissue. So far, therefore, the cavernous metamorphosis may be regarded as a secondary phenomenon; on the other hand, the intermediate tissue-changes are so decidedly characteristic of morbid growth that I cannot hesitate for a moment to place cavernous formations among the histioid tumours. Inasmuch moreover, as the process in question involves exactly the same tissue-changes as those which underlie the development of fibromata, and as the cavernous tumour, when freed from its contained blood, presents all the characters of a fibroid growth, I have chosen to deal with it here rather than elsewhere.

Fig. 52.



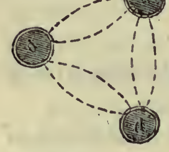
Fully-developed erectile tissue. $\frac{1}{300}$. From a cavernous tumour of the orbit.

§ 130. It is difficult to get an insight into the mechanism of a cavernous tumour. When any space contains a network or system of trabeculæ, that portion of the space which is not actually occupied by the trabeculæ themselves, must necessarily form another network or trabecular system. If we distinguish between a network and a parenchyma which occupies its meshes, each of these constituents must stand in the relation of a parenchyma to its fellow. The transverse section of any trabecula of one of the networks must be identical with the circumference of an islet of parenchyma as regards the other network, and *vice versâ.* Fibres which in one of the two networks surround the trabeculæ at right angles to their length, would, if they contracted, diminish the islets of the parenchyma of the other network, whose trabeculæ would in their turn become shorter and thicker. Fibres which correspond in their direction to the long axis of the trabeculæ of one of the two networks, would, if they contracted, increase the size of the islets of the parenchyma of the other network and render *its* trabeculæ thinner.

We may also suppose the entire mass of a trabecular network partitioned out into trabecular substance proper and tetrahedral or cubical nodal pieces (connecting pieces, Verbindungsstücke), common to three or four contiguous trabeculæ. Supposing the joint volume of the two networks to remain constant, and the trabeculæ of one network to become longer and thinner, this would necessarily entail on the one hand a diminution in the size of their own nodal pieces, on the other a shortening and thickening of the second network whose nodal pieces would simultaneously increase in size.

When once we have thoroughly grasped these rather difficult stereometric conceptions, we get at a very natural theory of the mechanism of cavernous metamorphosis. True, it is far from easy to conceive of a parenchyma traversed by an ordinary vascular network as being made up of a system of rounded trabeculæ enclosing meshes between them. This is made easier by imagining several vessels seen in transverse section (fig. 53*a*); the dotted curves (which may at the same time be supposed to represent the lines of contact of the capillary arches between *a* and *a*) would then indicate the transverse sections of the trabeculæ of parenchyma. The vascular network would thus be made up of long trabeculæ and small nodal pieces, the parenchymatous network of very thick but extremely short trabeculæ and nodal pieces of colossal size.

FIG. 53.



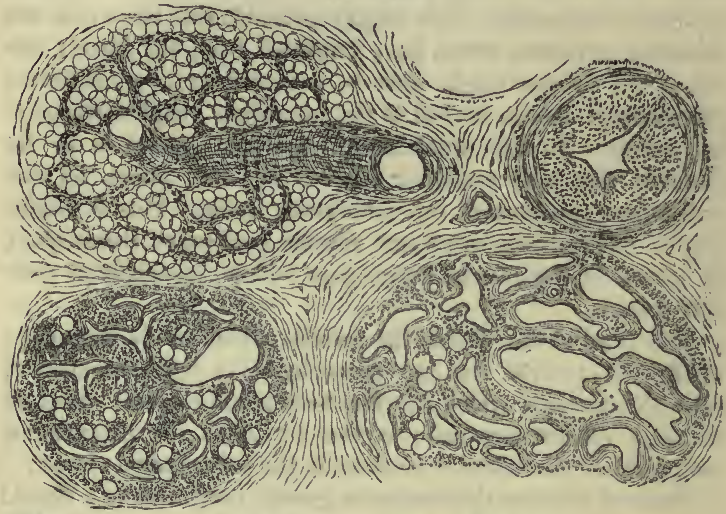
Now the cavernous metamorphosis is brought about as follows: in a circumscribed part of an organ, embryonic tissue is converted into spindle-cell tissue and fibroid connective tissue along the course of the vessels; this is followed by contraction taking place at right angles to the axis of the parenchymatous trabeculæ, in the direction therefore of the dotted curves (fig. 53), causing elongation of the trabeculæ, diminution in the size of their nodal pieces, and, as a necessary consequence, dilatation of the blood-channels; *i.e.* a shortening of the trabeculæ and an enlargement of the nodal points of that network which is constituted by the blood.

§ 131. Fig. 54 may serve to elucidate the above remarks; it represents the development of a cavernous tumour from adipose tissue. We see three clusters of fat-cells which correspond to as many stages of the cavernous metamorphosis. The least altered cluster exhibits the well-known capillary network, which is made apparent, in the present instance, not by injection, but by the walls of the vessels being coated with numberless round connective-tissue corpuscles. It is highly probable that these cells are colourless corpuscles which have migrated from the blood; this part of the process might then be regarded as a very insidious inflammatory change limited to the immediate neighbourhood of the vessels. In the adjoining cluster the process is so far advanced that only scattered fat-cells are still intact, all else having been transformed into embryonic tissue. This is beginning to undergo conversion into fibrous connective tissue along the course of the vessels, which gape widely, especially at their nodal points.

The third cluster shows the erectile tissue in its maturity; (cf. fig. 52); what was the parenchyma is now a system of trabeculæ, towards which the blood-containing spaces stand in the same quantitative ratio as that in which the parenchyma stood towards the vascular network in the least-altered cluster.

Thus we see that the cavernous growth originates in a fibroid degeneration of the capillary portion of the blood-path; it is a mistake therefore to derive it from an ectasy of the veins or arteries. This must not be taken to mean that the larger afferent and efferent vessels of the area undergoing degeneration remain unaltered. The arteries of the cavernous tumour more especially show an enormous thickening of their walls, a tortuous course, and a capacity for dilatation such as no healthy vessels, save the helicine arteries, ever exhibit. The annexed figure likewise informs us concerning their relation to the blood-spaces of the erectile tissue. They communicate with these spaces by as many apertures as there formerly were communications between the arterioles and the capillary network. The amount of blood in the erectile structure depends immediately on the degree in which the arteries are contracted. In fig. 54, besides the three degenerated clusters of fat-cells, we see an artery of larger calibre in transverse section. The vessel is firmly contracted; the intima, much thickened, is thrown into four longitudinal folds; the lumen is a mere slit; we can readily perceive how a farther contraction of the circular fibres would inevitably lead to its obliteration. I can assure the reader, that the very same artery, when fully dilated, would take up about twelve times as much space as it now occupies.

FIG. 54.



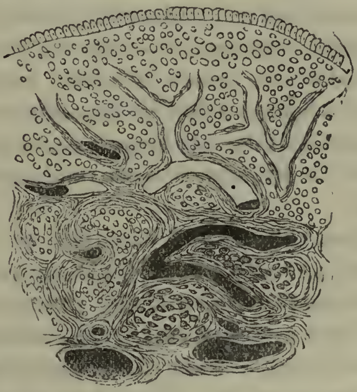
The development of a cavernous tumour in adipose tissue. Three clusters of fat-cells, representing the various phases in the development of the tumour; a divided artery is seen in the right upper corner. From the *panniculus adiposus* of the cheek. $\frac{1}{300}$.

Cavernous tumours originate by preference in the adipose layers of the organism. On one occasion I found cavernous metamorphosis going on in the interior of a lipoma. It *may* occur, as has been already said, in any organ of the body which possesses blood-vessels; in any organ therefore except cartilage, the cornea, and the vitreous humour. It is not unfrequently multiple. Cases are on record of a cavernous tumour of the skin having been associated with similar growths in the muscles and bones.

Cavernous tumours are occasionally malignant; but their malignity usually depends on a manifest complication with melanotic sarcoma, whose nodular foci are developed in the trabeculæ of the cavernous tumour.

§ 132. Cavernous metamorphosis of fibrous sarcoma itself is peculiarly interesting. *Billroth* was the first to speak of a "cavernous fibroid." I have already remarked, when speaking of the spindle-cell variety of sarcoma, that its vessels had as good as no proper walls, and therefore remained gaping on its cut surface. The same is true of the fibromata. Fibromata with exceptionally wide and gaping vessels may even appear quite spongy. *Billroth* found that naso-pharyngeal polypi, whose growth is peripheric, are especially prone to exhibit a cavernous *habitus;* and I can assert, from independent observation, that the cavernous tissue in such cases originates in precisely the same way as that which I have just described. Fig. 55 represents a vertical section through the circumference of a cavernous fibroid. Externally, we have a very vascular embryonic tissue; internally, the familiar trabeculæ of the cavernous tissue; while between the two are seen the transitional phases. I have placed cavernous tumours under fibromata on account of the identity of the histological processes which underlie the development of both; should any one doubt the adequacy of

Fig. 55.



Cavernous fibroid, after *Billroth*. $\frac{1}{300}$. (Naso-pharyngeal polypus.)

my reason, he may find an additional motive for conforming to my view in this second bond of union between the two forms.

b. *Lipomata or Fatty Tumours.*

§ 133. Not only is the lipoma or fatty tumour principally made up of the characteristic elements of adipose tissue, the fat-cells, but it also agrees in structure with the normal fat of the human body by the union of these fat-cells into little spheroidal clusters which are parted from one another by septa of connective tissue. A stouter coat of connective tissue combines several such clusters into a lobule, also of globular shape; and it is of such lobules that most fatty tumours appear to the naked eye to be made up. The *panniculus adiposus* also exhibits a lobulated structure, but its lobules (the *glandulæ adiposæ*) never reach the considerable dimensions which are commonly attained by the single lobules and tubera of a fatty tumour. The individual fat-cells of a lipoma differ in like manner from ordinary fat-cells. They are considerably bigger, *i.e.* more distended with oily matter, which in its turn is more fluid, and contains more elain than usual.

All the lipomata are perfect examples of central growth. Their enlargement, as well as their origin, depend in the last resort upon an abnormal production of new clusters of fat-cells; this is brought about by a moderate and sharply-defined proliferation of the connective tissue, leading to the formation of a circumscribed corpuscular aggregate, followed by an infiltration of the newly-formed cells with oily matter. It would seem however, that the formative stimulus is most intense amid a collection of pre-existing clusters; while it is certain that the vessels of the new clusters originate from the vessels of the older ones in the same way as do the vessels of papillomata. This explains why a lipoma is usually connected with neighbouring parts at one point only by a stout vascular pedicle, and has the rest of its external surface limited by a large-meshed connective tissue, or even by a smooth capsule; this explains its peculiar, lobulated build—in a word, the central growth of the tumour.

Lipomata occur by preference in those localities which are normally infiltrated with fat, such as the subcutaneous, submucous, subsynovial, subserous, subfascial, intermuscular, and intraorbital connective tissue. From this point of view the lipomata may be regarded as overgrowths of the normal layers of fat, *excrescentiæ membranæ adiposæ* (*Morgagni*); and if we choose to regard these layers as a connected system of adipose tissue, and not as a certain quantity of connective tissue infiltrated with fatty matter, we may claim for lipomata, together with polysarcia, the quality of hyperplastic tumours. For my own part, I look upon polysarcia as a fatty infiltration of pre-existing connective tissue, and on lipoma as a fatty infiltration of a growth of independent origin and development.

§ 134. The lipomata, like the papillomata, at first increase slowly, their growth proceeding in an accelerating ratio. They may attain a very considerable size. Tumours as large as a man's head and larger, are by no means rare. Moreover their central mode of growth involves their speedy emergence from the surrounding soft parts, and their protrusion towards the nearest free surface; they push the skin before them, and finally project above the surface as tuberous or polypoid excrescences.

The greater the size of a lipoma, the greater the probability that farther metamorphoses have taken place in its interior. We not unfrequently find a chronic inflammatory overgrowth and fibroid transformation of the interstitial connective tissue. In consequence of this the clusters of fat-cells perish *en masse*, the remaining lobules being separated by broad bands of fibroid tissue (Fibroid Lipoma, *Steatoma Mülleri*). Retrograde changes are more commonly met with. *Calcification* of the fibrous matrix of the clusters stands foremost among these. It results in the formation of a spongy calcareous framework with exceedingly fine meshes, which permeates the entire tumour, or large sections of it, making it very hard and heavy. Yet more remarkable is the *mucous* transformation of the tissues of a lipoma, and the consequent possibility of a fatty tumour being converted into a myxoma. In persons who are much emaciated, who have been exhausted by lingering disease, we often find the adipose tissue about the heart deprived of its fat, and in a peculiarly swollen and œdematous state, which, on minuter examination, proves to be due to mucous infiltration. Precisely the same phenomenon is met with in lipomata, and especially in the larger, pedunculated lipomata of the skin. The tumour acquires a transparent and colourless aspect; it becomes tremulous and jelly-like; the fluid which oozes from its cut surface contains mucin; so that we are compelled to acknowledge the myxomatous character of the growth, and to call it (should the entire tumour have undergone this degenerative change) no longer a lipoma, but a myxoma.

Lipomata, in common with fibromata, are very justly regarded as decidedly benign. A lipoma, once thoroughly extirpated, never recurs; metastases to neighbouring lymphatic glands or to internal organs have never been observed.

c. *Enchondromata or Cartilage Tumours.*

§ 135. The term enchondroma is applied to cartilage when it appears in the form of a tumour at some point in the body where no cartilage should normally exist. The substance of an enchondroma therefore presents the peculiar elastic hardness, and the milk-white colour, translucent in thin layers, which are characteristic of cartilage. As regards minute structure, normal histology, as everybody knows, distinguishes between several varieties of cartilage; and particularly between *hyaline cartilage*, whose matrix is homogeneous, and *fibro-cartilage*, whose matrix is fibrous. But the cornea also yields chondrin on boiling, and its tissue may very well be regarded as a form of cartilage, whose cell-containing cavities are stellate, with branching processes (*cartilage with stellate cells*).

All these textures may coexist in an enchondroma, yet hyaline cartilage as a rule predominates. One of the most characteristic and most frequent combinations is that of small rounded islets of hyaline cartilage passing at their periphery into fibro-cartilage or corneal tissue. The *hyaline cartilage* forming the nucleus of each islet differs in no respect from the well-known physiological type. The cells are either single, or arranged in pairs or groups, showing how the limits of each primary element have been extended by subsequent endogenous proliferation. The capsules are not always distinct; their entire absence is a sign that the matrix is beginning to soften. The protoplasm of the cells is of variable form. It is usually stellate, and contains a nucleus; this form may either be due to shrinking of the cells under the influence of reagents, or to the spontaneous contractility of the protoplasm; the latter explanation being especially applicable when a conversion of the hyaline cartilage into mucous tissue is taking place. Under such circumstances, the formation of processes coincides with the disappearance of the capsules, and a mucous intumescence of the matrix. *Virchow* has observed cells with processes of colossal length in an enchondroma undergoing this change (*Virchow's Archiv*, 28, p. 238). Towards the periphery of these islets of cartilage, the cells decrease in size, they become flat and lenticular; the matrix shows striæ, and is traversed by fibres of variable thickness, which resemble elastic fibres and are remarkable for their stiffness (*fibro-cartilage*). Or else the cells may become spindle-shaped and stellate, they may anastomose with one another, and be obviously situated in a lacunar system provided with nodal points, while the intercellular substance retains its homogeneous and transparent quality (*cartilage with stellate cells, corneal tissue*). Neighbouring islets of cartilage are in contact by these outermost zones of fibro-cartilage or cartilage with stellate cells, and are thereby united into groups, forming nodules or lobules as large as a pea, of which the entire tumour appears to the naked eye to be made up.

§ 136. The above sketch of the microscopical appearances shows that enchondromata are also endowed with a lobulated structure; but their lobulation differs very essentially from that of a lipoma, or even from that of a papilloma. The lobules of an enchondroma are co-ordinate with one another; they have grown up side by side; it is only this topographical juxtaposition of the lobules, and not any higher unity, such as a common vascular apparatus, or a growth by development *ab intra*, which unites them into a single whole. Although it is noteworthy, as seeming to point to an organic type of structure, that the individual lobules of which an enchondroma is made up, never exceed a certain size, yet this is explained by the simple fact, that cartilage generally—even in the normal course of development—is not deposited in continuous masses of large size, and—to use a teleological form of expression—*ought* not to be so deposited. Cartilage being a non-vascular tissue, is nourished by the transmission of nutrient fluid from cell to cell. At a certain distance from the vessels which carry the blood, this mode of nutrition becomes impossible; and unless some new arrangement be provided for the supply of the central parts, disturbances of nutrition in those parts must inevitably follow any farther growth. In the development of the osseous system from cartilage we accordingly find a singular arrangement. When a cartilaginous epiphysis has reached a certain bulk, medullary spaces containing blood-vessels appear exactly in its centre; and this gives the necessary impulse for the development of true bone, which accordingly begins at this very point (epiphysal nucleus). The formation of vessels and of true bone has also been observed in enchondromata. It is the rule nevertheless, that the individual portions of cartilage should never reach a size so great as to interfere with their being conveniently nourished from their circumference.

§ 137. This implies of course that the connective tissue which combines the lobules of the enchondroma into a tumour (the stroma) contains an adequate number of vessels, and that a sufficient quantity of blood passes through those vessels. This is the case in tumours of relatively small size, and at the circumference of the larger ones as well. But it is not the case in the interior of the latter. On the contrary, the vessels appear to be compressed and obliterated by the pressure of the growing tumour. In every enchondroma of considerable size—and some have been met with weighing five pounds—we may accordingly assume that a more or less complete obliteration of the vessels in its interior has taken place, giving rise to subsequent metamorphoses of its substance.

We nearly always find *calcified* patches in an enchondroma. The cartilage then exhibits the infiltration which has been described at length in § 49. This starts now from the matrix, now from the cells and capsules. The results are always the same to the naked eye; the colour of the infiltrated parts becomes dark-yellow and opaque, their consistency granular and friable. It has already been mentioned that this calcification may occasionally be followed by a true ossification, as in the normal development of bone. Reference has also been made to the conversion of the cartilage into *mucous tissue.* This should be regarded less as a degenerative process, than as a change of type, as a conversion of one tissue into another tissue of equivalent quality, which may result in the partial or complete transformation of an enchondroma into a myxoma. It is far otherwise with that softening of an enchondroma which begins with a fatty metamorphosis of the cartilage-cells, their conversion into granule-cells, &c., these changes being farther complicated by a mucoid softening and solution of the matrix; the final result of the process being the formation of cavities, fluctuating points—in a word, of "cysts due to softening"—in the interior of the enchondroma, which are filled with a jelly-like viscid fluid containing a very large proportion of mucin. This *cystoid degeneration* of enchondromata (*enchondroma cysticum*) ought certainly to be regarded as a consequence of impaired nutrition.

§ 138. Unfortunately however, this is not the last of the anatomical modifications of enchondroma. The complication of enchondroma with alveolar sarcoma (vulgarly called cancer on account of its alveolar structure) has yet to be considered. It is to this complication that enchondroma owes a certain reputation for malignity, a reputation which the growth *per se* does not deserve. Cases are on record of medullary tumours appearing at the seat of operation and in other regions of the body after the removal of enchondromata; such cases all refer to this combination of enchondroma with soft sarcoma. In such cases too, the superadded element of malignity can usually be recognised even in the primary tumour. Medullary nodules of variable size are met with along the vessels in the stroma of the cartilaginous tumour. Still, it is an established fact that pure enchondromata are also liable to recur; a gradual extension of the growth along the lymphatics, metastases to the nearest lymphatic glands, nay, even to internal organs, have more than once been observed. Among internal viscera the lung is the favourite locality for secondary deposits of an enchondromatous nature. It must be remembered, however, that these secondary deposits are excessively rare, and always of extremely small size, even when the dimensions of the primary tumour were colossal.

§ 139. From a quarter to four-fifths of all enchondromata occur in the osseous system, and more particularly in the diaphyses of the long (tubular) bones. We shall hereafter become acquainted with the great variety exhibited by enchondromatous tumours of bone, both in the manner of their first appearance, and in their subsequent development; here I will only allude to a single variety, the *osteoid-chondroma* of *Virchow*, inasmuch as it familiarises us with an essentially aberrant form of cartilage as its main constituent. In reckoning up the various kinds of cartilage, one tissue is usually omitted, which nevertheless possesses the most substantial claim on our notice on the ground of its morphological constitution. I allude to that peculiar sort of connective substance (Bindesubstanz) which is called true bone after it has been impregnated with calcareous salts, but which, before this impregnation, consists of a highly-refracting, dense and homogeneous matrix, in which the future bone-lacunæ still exhibit more of a rounded or rather perhaps of a polygonal form, with very short processes. The trabeculæ of an osteophyte (*see* Diseases of Bone) are composed of this tissue; in thin layers, it lines the medullary spaces of such bones as are passing from the spongy to the compact state. It plays a great part in the repair of fractures by forming the main bulk of what is known as "callus." Its truly cartilaginous properties are however especially manifest when, as in the osteoid-chondromata, it forms tumours, often of colossal size.

§ 140. Osteoid cartilage may also originate independently of the bones; in a compound tumour from the back, *Virchow* found portions of well-marked osteoid cartilage side by side with myxomatous and lipomatous elements; but as a general rule such tumours spring from bone. Their growth begins between the periosteum and the surface of the bone, but they subsequently penetrate through both the periosteum and the compact cortex. They usually present themselves as fusiform or pear-shaped swellings of one of the extremities of a long (tubular) bone. They have been most often met with in the humerus and femur. Retrograde metamorphoses are less common in these than in any other of the heteroplastic tumours which we have hitherto considered. This immunity is connected with the very complete and uniformly efficient vascularisation of every part of the tumour, an advantage which the osteoid-chondroma enjoys in common with osteophytes and callus. The cartilaginous trabeculæ of the osteoid substance form a delicate framework, in whose meshes even the finest capillaries are free from all risk of being squeezed by the growing tissue. One metamorphosis only, and one which might be anticipated *a priori*, is met with in nearly every osteoid-chondroma; I mean a transition of its proper tissue into that of true bone. Hence it is that an osteoid-chondroma creaks under the knife, and that we are sometimes obliged to have recourse to the saw in order to divide it. The ossified portions are known at once on the cut surface by their great firmness and density; should the entire tumour have been converted into bone, the osteoid-chondroma is said to have become an *osteoma.*

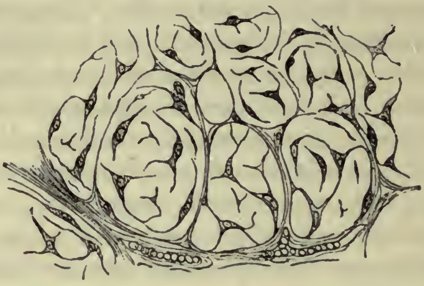
As regards its innocence or malignity, we cannot venture to pronounce any decided judgment, owing to the small number of cases which have been hitherto recorded. The elements of prognosis laid down for enchondromata may be held (at least provisionally) to be applicable to this variety likewise.

d. *Myxomata or Mucous Tumours.*

§ 141. A summary of all that has been said in the sections treating of mucous tissue shows us that, although it is to be regarded as a thoroughly independent and vitally active member of the connective series, it nevertheless originates, in the vast majority of cases, by a secondary metamorphosis of other connective substances (§ 42) entering into the formation of tumours. We have become acquainted with a myxomatous variety of sarcoma, lipoma, and enchondroma respectively, understanding thereby tumours, circumscribed patches of whose proper substance had undergone conversion into mucous tissue. It must be admitted that this order of sequence is an inference from the coexistence of these modifications; but the possibility of a myxomatous metamorphosis of cartilage, adipose tissue, and areolar connective tissue, has been established by observations so numerous and well authenticated, that we are quite justified in assuming the sequence to have been such as we have stated, and not of an inverse order; moreover, we have good grounds for preferring such a conclusion (at least in the majority of instances) to the hypothesis of a simultaneous development of compound types of tissue. Bearing this well in mind, it seems at least prudent to restrict the term "mucous tumour" to such growths only as are exclusively made up of mucous tissue. Such tumours indeed are not common; they are common enough however to warrant us in maintaining the group of *myxomata* as originally constituted by *Virchow.*

§ 142. The definition of mucous tissue implies the existence only of a basis-substance containing mucus, or of one which has undergone mucous softening; it involves no theory concerning the form and character of the cells; it allows us therefore to set up a certain number of histological subspecies of the myxoma. The optical and physical properties of mucin are (§ 39) best displayed when the number of cells, whether round or stellate, is small in proportion to the amount of intercellular substance. Accordingly the *hyaline myxoma* (fig. 56) is the most characteristic form of the entire group; it is colourless, translucent, like a tremulous jelly. Should the cells predominate, either in the entire tumour or in single portions of it, we get a whitish, marrowy condition—*the medullary myxoma.* Fatty infiltration of the cells leads to the formation of a *lipomatous myxoma* (m. lipomatodes).

FIG. 56.



Hyaline myxoma of the subcutaneous connective tissue near the angle of the jaw. $\frac{1}{300}$.

§ 143. The myxoma, like the lipoma, has a lobulated structure; it is made up of separate parts of variable size, which are separated from one another by partitions of connective tissue. Little is known at present concerning the arrangement of its blood-vessels; injections of a hyaline myxoma of the cheek (as large as a closed fist) made by myself, lead me to suspect that myxomata are but sparingly provided with capillaries, that their vessels are mainly of largish calibre, and run in the thicker septa.

Myxomata form nodular swellings which increase rapidly in size; owing to this circumstance, as well as to the great softness of their tissue, they are often mistaken for soft cancer. They resemble lipomata in making for the surface by the shortest or easiest route; here they form nodulated or fungous projections, and may even become pendulous or polypoid.

The subcutaneous areolar tissue of the thigh and back, and of the external genitals in the female; the intermuscular connective tissue of the neck and face, are the favourite seats of myxoma; next to these, it is most frequently met with in the bones and nervous system. In the nervous system (according to *Virchow*) it is often multiple, myxomatous nodules being formed at several points at once in the connective tissue of the perineurium. As regards prognosis, myxomata, if we succeed in duly eliminating the myxomatous variety of sarcoma, may be classed among benign tumours. They do not recur after radical extirpation.

e. *Osteomata or Bony Tumours.*

§ 144. Bony tumours in some respects resemble myxomata. Bone, though a living constituent of the body, and even susceptible of undergoing metamorphosis, resembles mucous tissue in being a "terminal" tissue, *i.e.* it usually winds up a series of other metamorphoses. The stromata of cancers may undergo ossification. *Lücke* has actually recorded a case of epithelial cancer with a bony stroma; we are acquainted with an ossifying sarcoma; enchondromata and osteoid-chondromata may be converted into bone; even the septa of connective tissue between the lobules of a lipoma may become ossified; we are therefore obliged to repeat what was said in defining a myxoma, limiting the term osteoma to such tumours only as consist throughout and in all their parts of bone-tissue. If we distinguish with *Virchow* between a hyperplastic and a heteroplastic form of osteoma, we shall have to include under this head whatever tumour-like overgrowths of the bones we may come across. Heteroplastic osteomata are undoubtedly very rare.

f. *Myomata.*

Under this name we include all tumours which are mainly composed of true muscular fibre. According as the muscular fibres belong to the smooth or the striped variety, we follow *Zenker* in distinguishing between *leiomyomata* and *rhabdomyomata*. I have found however, that it is just in the case of tumours that transitional forms between smooth and striped muscular fibre are to be met with. A large myoma of the retroperitoneal adipose tissue which I had an opportunity of examining, was made up of transversely striated spindle-shaped cells; so too, a myoma of the vaginal mucous membrane, which showed an obstinate tendency to recur. Pure leiomyomata, when they occur in the bowel, the urinary bladder, &c., exhibit throughout the structure of muscular membranes. I assert boldly that no one who has once investigated a tumour of this kind is ever likely to confound simple spindle-cells with muscular fibre-cells. The remarkable uniformity in size and appearance of all the cells and nuclei, enabling them to unite closely into fibrous bands of very elegant texture, has something extremely distinctive about it. The naked-eye appearances, the interlacement of the fibrous bands, unquestionably remind one of the fibromata; but I have never been able to recognise the existence of a fibro-muscular tumour in *Virchow's* sense of the word. In a myoma of the testicle, I found groups of ganglion-cells, and stroma-fibres. (*See* Testicle.)

g. *Neuromata.*

§ 145. The term neuroma is used to denote any histioid tumour which may happen to be intercalated in the course of a nerve-trunk; it is employed with especial frequency to denote fibromata and myxomata; hence we must distinguish *in limine* between *false* neuromata, such as these, and the *true* neuromata, which consist chiefly of newly-formed nerve-fibres and ganglion-cells. A tumour of this sort, as large as a hen's egg, situated in the retiring angle between the ribs and the anterior circumference of the vertebral column, has recently been observed (*Schmidt*, Frankfurt-am-Main). It merits especial notice, inasmuch as it seems to be the first recorded example of a true neuroma not of hyperplastic origin. True, its situation does not absolutely exclude all possibility of its having originated by overgrowth of a sympathetic ganglion; should this be its true character, it would come under the same category as those circumscribed overgrowths of the greater cerebral ganglia (thalamus opticus, corpus striatum) which have been more often met with, as well as those fusiform enlargements of the peripheric nerve-trunks, consisting of nerve-fibres, which *Virchow* has described under the name of true neuromata.

h. *Compound Histioid Tumours.*

§ 146. In all the histioid tumours which we have hitherto examined, a single tissue could, with more or less of certainty, be viewed as the dominant constituent, thus enabling us to decide on the character of the growth, and to give it an appropriate name. There can be no doubt however that compound tumours exist as well. When distinctly cartilaginous elements are found associated with lipomatous ones, when sarcomatous nodules are found (*see* above) scattered through an enchondroma, we are puzzled whether to call these things enchondroma lipomatodes or lipoma cartilagineum—sarcoma cartilagineum or chondroma sarcomatosum. This perplexity recurs when we come to inquire into the clinical character, prognosis, &c., of such tumours. As regards the latter question, we are justified in laying down the following propositions on the basis of several reliable observations: 1st, that the prognosis of compound tumours is less favourable than that of the several species of which they are made up; 2nd, that the presence of sarcomatous constituents renders a compound tumour at once equivalent to a sarcoma. A compound tumour of this sort usually shows its true colours by recurring as a sarcoma after its first extirpation. (For the combination of histioid growths with carcinoma, *see* under the head of Carcinoma Sarcomatosum.)

4. Morbid Growths due to Abnormalities of Epithelial Development, whether involving the conjoint Blood-vascular and Connective-tissue System or not.

§ 147. The present section will be mainly devoted to the enunciation of some general views concerning the essential nature, the mode of origin, and the affinities, of the so-called "carcinomata." By carcinoma we understand a morbid growth which exerts a destructive action upon the organs of the body, which usually recurs after extirpation and gives rise to secondary deposits, and which is therefore of a malignant nature. These properties indeed, as we have seen already, are likewise exhibited by certain histioid tumours, and it would be exceedingly desirable to have some definite anatomical criterion, by which we might recognise carcinoma as such, and distinguish it from other destructive and malignant growths. Now it has been, and still is usual, to regard a certain morphological peculiarity, what is known as the alveolar type of structure, as essential to the recognition of "cancer." This means no more than that we look for the essence of cancerous degeneration in the development of circumscribed deposits of cells, which burrow their way in certain directions, and necessarily convert the residual parenchyma of the organ which is undergoing destruction into a trabecular framework or stroma, the form and size of whose meshes (alveoli) are regulated by those of the cellular aggregates which they include. It is obvious that this plan of structure is peculiarly adapted for the accommodation of large multitudes of free cells; and such an adaptation we must regard (in conformity with what was said in § 121) as the most powerful cause both of the local growth of a tumour and of the infection of the entire organism. This justifies the seemingly arbitrary selection of the alveolar type of structure as the anatomical mark of cancer; but a new difficulty starts up when we come to reflect that the term "carcinoma" will also have to include the alveolar sarcomata; tumours, in whose "interpenetration with cellular aggregates" we preferred to see an analogy with the suppuration of inflamed tissues. I accept this consequence as logically inevitable, and I therefore range myself on the side of those who regard "carcinoma" as a term essentially clinical, finding but an imperfect anatomical expression in that alveolar type of structure with which it is invariably associated.

§ 148. The vast majority of carcinomata originate primarily either from the epithelium which covers the free surfaces of the body, the skin and mucous membranes, or else from the secreting glands. They depend upon an abnormal growth of the epithelial tissue. We might go so far as to say that the process which underlies all these carcinomata is an ingrowth of the epithelium into the sub-epithelial stratum of connective tissue, whether of the skin or of a mucous membrane, or into the interstitial connective tissue of the glands. The manner in which this ingrowth takes place differs widely in different cases. The general impression conveyed by carcinomatous destruction, *e.g.* the appearances presented by a vertical section under a low power, seems to justify the assumption that it consists in a morbid imitation of that histological process which precedes the development of the open glands. In both cases alike, we have aggregates of epithelial cells projecting in the form of tap-shaped processes or cords from the under surface of the epithelium, and boring their way between the fibrous bundles of the connective tissue. Phenomena of active fission are also seen to take place in the elementary constituents of these cellular aggregates; two leading features therefore are undeniably common to the morbid process and the normal development of glands. Nevertheless the view which makes the development of cancer consist in a lawless and irregular counterfeit of the normal growth of glands (*hétéradénie* of the French) is only legitimate within certain limits. After having devoted so much time and space in former chapters to the consideration of the normal growth of epithelium, it would be unfortunate indeed were we now to sacrifice the fruit of those considerations, by a premature attempt at systematisation. Indeed, as regards cancerous disease of open glands, special stress must be laid on the fact that every imaginable intermediate stage exists between simple glandular hypertrophy and glandular cancer. Of late years, our knowledge of these transitional forms has been much extended, and the term adenoma has been proposed for a tumour which is neither simple hypertrophy nor yet cancer. Such at least is the most commonly received acceptation of the word; some authors raising the denotation of the term in the scale, while others lower it, the former placing it nearer to hypertrophy, the latter to carcinoma; and that any such shifting should be possible affords conclusive proof of the existence of a graduated scale between the two extremes of simple hypertrophy and cancer.

A general appreciation of those cancers which spring from the epidermis or the epithelial covering of mucous membranes is far more difficult. Here too the hyperplastic and carcinomatous conditions are unmistakeably correlated. It is matter of experience, *e.g.* that those circumscribed hypertrophies of the skin which we call warts and papillomata, are capable of passing into epithelial cancer. The transition, as regards its purely anatomical features, takes place as follows:—The hypertrophy of the papillæ occasions a more or less considerable dislocation of the plane along which the epithelium and the connective tissue are in contact. The steep sides of the overgrown or newly-formed papillæ bound deep fissure-like depressions. Accordingly the epithelial coat of the papillæ is at the same time the epithelial lining of the interpapillary fissures; and so long as this condition is maintained *in statu quo* by an adequate shedding of the older epithelial cells, the growth preserves its hyperplastic character. The longer the papillæ become, however, more especially if they break up into dendritic vegetations, the greater must obviously be the impediment to the adequate removal of the older cells. The lateral pressure exerted by the apices of the papillæ, whose terminal ramifications spread out widely, while they rest upon a very narrow base, shuts in the interpapillary fissures from above and consequently determines a gradual and progressive accumulation of epithelial elements in their interior. In the deeper parts of the tumour, the epithelium soon ceases to be a mere lining; it forms a solid mass which fills the interpapillary fissures. In this capacity it now begins to burrow at various points into the underlying connective tissue. Elongated cylinders of epithelial cells make their appearance; at first, they simply project into the cutis from the under surface of the epidermis; subsequently penetrating more and more deeply into it. The carcinomatous condition is thereby definitely established. It were indeed impossible to overlook the resemblance between these tap-shaped epithelial ingrowths, and those which take part in the development of glands; moreover, as has been already stated, the constituent cells are seen to undergo active fission; nevertheless, I shall continue to maintain, until the contrary has been proved, that their growth, like that of normal epithelia, is primarily due to a peripheral apposition of young cells; and this hypothesis seems to me quite as plausible as that of the enlargement of retention-cysts by secretion from their walls. The fissiparous multiplication which takes place in the interior of the epithelial sprouts is indicative of a secondary growth; it may even contribute most to their increase in thickness; but it has no share in their elongation, in that inward growth of the sprouts, to which the destruction of the affected organs is actually due. This subject will be more fully treated in the sections devoted to squamous epithelioma; the object of these preliminary remarks being to direct attention to the fact that the laws of normal growth retain their force even in these most extreme and perilous departures from the normal type.

I. Glandular Carcinomata.

§ 149. Is there any such thing as an undoubted true hypertrophy of glands? If our definition of "true glandular hypertrophy" involves—1st, an absolute agreement with normal glands in structure and composition; 2nd, a proportionate increase in functional activity—then indeed the term would have to be confined to the hypertrophy which the mammary gland undergoes during lactation, and to those uniform enlargements of one kidney, or of single lobes of the liver, which have long been known as "compensatory hypertrophies," inasmuch as they usually follow obliteration of the other kidney, or of the remainder of the hepatic parenchyma. In such cases the tubuli uriniferi are elongated, the number of hepatic cells in each acinus is increased, and the capillary network undergoes a corresponding extension; so that it is only with the naked eye that we can estimate the increased bulk of the renal fasciculi or of the hepatic lobules, the microscope serving merely to establish their perfect conformity to the normal type. As regards the hypertrophy of the mammary gland in lactation, I must refer the reader to the appropriate sections of the Special Part of the present work.

§ 150. All other forms of so-called glandular hypertrophy diverge in some way or other from the normal standard. First, we have a group of cases, with regard to which we are never sure what proportion of the total enlargement should be ascribed to morbid overgrowth of the gland-tubuli, and what to their coincident dilatation. To this group belongs the hypertrophy of the mucous follicles in catarrh of the stomach and large intestine, of the trachea and bronchi. The proliferation of the subepithelial layer of connective tissue which invariably accompanies every catarrhal inflammation of a mucous membrane leads to compression and closure of the ducts which penetrate it, and so hinders the free discharge of the secretions; a certain degree of dilatation of the follicles, due to retention of secreted matters, thus contributing to the gross result. As compared with this, the independent growth of the glands, *i.e.* the growth due to fission of their epithelial elements, plays a more or less subordinate part. It may confine itself to furnishing the necessary epithelial lining for the gland as it gradually degenerates into a mucous cyst. Cases of this sort are analogous to atheromata of the sebaceous glands, in which we undoubtedly have more epithelium than is strictly required to line the cavity of a sebaceous follicle, but never—unless the atheromatous cyst has become an epithelial cancer—any centrifugal budding forth from the epithelial layer.

§ 151. Connected with the above are cases in which an independent outgrowth of the secreting parenchyma undoubtedly takes place, but in which we may reasonably hesitate before we regard the newly-formed tubuli as true, *i.e.* as functionally capable portions of the gland. Both the sebaceous and the sudoriparous glands may undergo a monstrous excess of development in circumscribed portions of the skin, and (especially the former) form fungous tumours of great size, without any increase in the amount of secretion being observable on the surface. In the hypertrophy of the sebaceous glands moreover there is a marked deviation from the normal plan of structure, viz. a thickening of the connective tissue of the follicular sacs. A farther extension of this peculiarity leads to subepithelial sarcoma of the glands, *e.g.* of the female breast, a form of disease to which *Billroth* has on this account applied the name of adenoid sarcoma.

§ 152. With the complete emancipation from the physiological purpose of gland-growth begins the domain of those tumours which I call ADENOMATA. Apart from its stroma, the adenoma consists of epithelial cells, whose arrangement at once recalls the epithelial lining of the tubular or acinous glands. The cells are, for the most part, grouped round a central axis, as though they really included a tubular lumen; but the lumen itself is either wholly wanting, or present only in an interrupted form, plugged with mucous or colloid matter, and most assuredly shut off from free communication with the efferent duct of the gland. It would seem as though Nature had concerned herself mainly with an unlimited production of new glandular tubuli, without much caring what became of them. She seems to forget that a proportionate development of blood-vessels and connective tissue is indispensable for the due perfection of a glandular parenchyma; and so, as the process continues, a tumour extraordinarily rich in cells is formed, too scantily provided however with vascular connective tissue to enable its nutrition to be adequately carried on throughout its entire substance, and which therefore evolves within itself the causes of its own ultimate destruction.

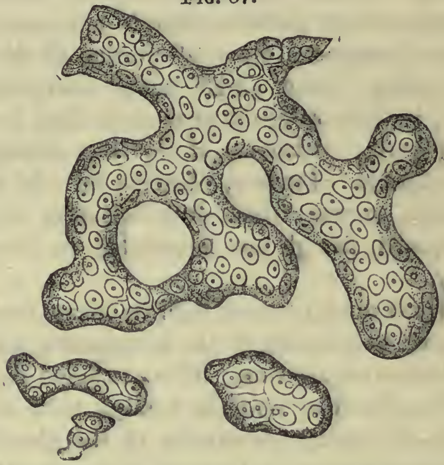
We are at present acquainted with adenomata of the liver, mammary gland, sebaceous glands (Lupus), and the mucous follicles of the rectum. It is only in the last-named case that we find it hard to separate adenoma from columnar epithelioma (Cylinderepithelialkrebs). (*See* below.) As for the rest, we find practical means of distinguishing them from cancer, partly in the manner of their development, partly in their clinical history. Adenoma forms globular, sharply-circumscribed nodules, which replace a comparatively small portion of the gland from which they spring. Each single nodule increases by central proliferation; it tends rather to push aside than to infiltrate the neighbouring parts. Adenoma of the liver actually surrounds itself with a capsule. Further, adenoma is to be regarded as a tolerably benign growth, which does not recur or give rise to secondary deposits, though our knowledge on this point is still in its infancy.

§ 153. Glandular cancer, with its many varieties, constitutes the natural termination of the histogenetic series which we have been hitherto considering. If we imagine the independent growth of the glandular epithelia waxing more luxuriant and more general, the regular elaboration of the gland-tubuli being more and more neglected for the sake of a proportionately more rapid penetration of the interstitial and surrounding connective tissue, we shall have a tolerably correct notion of glandular cancer. Its individual features however demand a more detailed examination.

That the growth originates in the glandular epithelia has been recently established by numerous observations. The cells divide and multiply. The first result of their multiplication is an obliteration of the lumina of the respective tubes and acini, which are converted into solid groups of cells. These immediately proceed to put out buds in all directions, which bore their way into the neighbouring connective tissue. This is the common starting-point of the many varieties of glandular cancer, the more important of which will now be described *seriatim*.

§ 154. Soft cancer (carcinoma medullare, encephaloides—hitherto often confounded with the soft variety of alveolar sarcoma) produces cancer-cells in the greatest number, though not always of the greatest size. Their round, vesicular nuclei, furnished with distinct, lustrous nucleoli, prove that these cells are truly descended from the mucous layer of the blastoderm; they form elaborately twisted cylinders beset with clavate appendages which are best seen when the juice squeezed from the cut surface of a recent specimen (cancer-juice) is examined in serum (fig. 57). In these cylinders the boundary-lines between the individual elements cannot be detected. This is because the protoplasm of the cells is absolutely naked, so that their immediate juxtaposition produces the optical effect of continuity. It would seem as though the speedy onset of fatty metamorphosis hindered the farther evolution of the epithelial type, for we seldom come across a cell of large size whose protoplasm does not already contain one or two oil-globules. The greater the number of oil-globules, the more distinctly can we trace the outlines of the cell, which are otherwise so difficult of demonstration. The conversion of the cells into granule-corpuscles with fatty *débris* appears to take place in the usual way. Neither microscopical nor chemical investigation has yet succeeded in showing the existence of any specific elements in cancer-juice. The clear and colourless serum contains albuminates and albuminoid matters in solution; among these there may perhaps be

FIG. 57.

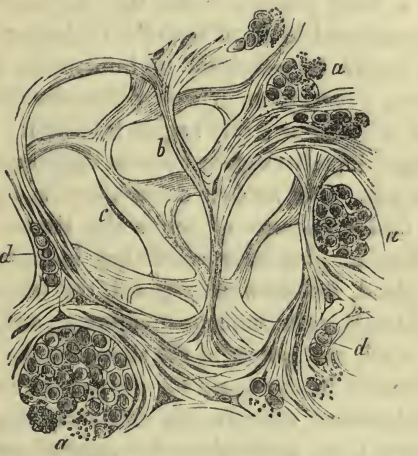


Cellular aggregates from the juice of a soft cancer of the breast. After *Billroth*.

some ferment-like bodies, which are at present however wholly unknown.

§ 155. On examining what is left after the cancer-juice has escaped, on exploring the spaces in which the juice was contained, we are confronted by the second element in every cancerous formation, the cancer-stroma (fig. 58). To demonstrate the stroma as perfectly as possible it is necessary to cut fine sections from various parts of the tumour, which must then be pencilled out; a framework of connective tissue is thus displayed, whose trabeculæ enclose oval spaces; the shortest diameters of these spaces being at least twice the breadth of the stoutest of the trabeculæ, and at least five times the breadth of those of medium thickness. This implies that neither the thickness of the trabeculæ nor the size of the meshes are the same in all cancers, but that a certain ratio may be said to exist between the width of the trabeculæ and that of the meshes. This ratio is of value in distinguishing the individual varieties of cancer from one another.

Fig. 58.



Stroma of soft glandular cancer pencilled out. *a.* Cylinders of cancer-cells seen in transverse section; *b.* Trabeculæ of stroma; *c.* A solitary spindle-cell which stretches obliquely from one trabecula to another, and serves, by deposition of basis-substance along its protoplasm, to give the impulse for the formation of a new trabecula; *d.* Round-cells infiltrated into the substance of the trabeculæ. $\frac{1}{300}$.

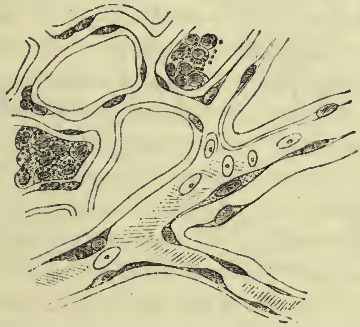
As regards minute structure, the thicker trabeculæ of the stroma usually consist of a striated connective tissue in which a large number of spindle-shaped cells are embedded. These trabeculæ are not circular, but triangular, quadrangular, or polygonal in transverse section, the sides appearing concave, the angles pointed. The latter are occasionally produced into thin membranes, which stretch across the whole or a part of a mesh. The general impression left on the observer's mind is that of a progressive rarefaction of the stroma by the growing contents of the alveoli; and this impression may be unconditionally accepted, at least as regards the earliest stages in the development of cancer, when the growth is still confined within the lobules of the gland. At a later period, when the degenerated lobes and lobules have coalesced to form nodules of larger size, and these have already begun to penetrate by infiltration into the neighbouring tissues, a formation of new trabeculæ takes place in the older parts of the tumour; this begins by solitary spindle-shaped cells becoming obliquely stretched across the larger alveoli, where they serve as guiding or nuclear centres for the subsequent apposition of the basis-substance of connective tissue.

The soft form of glandular cancer has hitherto been found in the salivary gland, the mammary gland, the testicle, ovary, prostate, thyroid body, nasal mucous membrane, and liver. In what measure, if at all, soft cancer of the stomach may originate in the follicular structures must remain for the present an open question.

The soft glandular cancers are extremely malignant; particularly because they undermine the general nutrition of the organism more rapidly than any of the other forms, and so prove fatal by the cachexia to which they give rise. Metastatic deposits are only found as a rule in the corresponding lymphatic glands.

§ 156. THE TELENGIECTATIC CARCINOMA (a variety of the so-called fungus hæmatodes). Inasmuch as blood-vessels form an integral part of the stroma of every gland, and this stroma, as we have seen already, undergoes direct conversion into the stroma of the glandular cancer, it is easy to see that every such cancer must, at least in its earlier stages, contain blood-vessels. In a general way these vessels may be said to share the fate of the stroma, *i.e.* they undergo rarefaction so long as epithelial proliferation is in the ascendant, and when its products are softened and disintegrated by fatty metamorphosis, the vessels may even take on an exuberant development. Some cancers there are however—and these may rightly be termed telengiectatic—in which the development of vessels predominates from the very first. In a cancer of the testicle whose growth was extremely rapid, I found the stroma wholly made up of vascular ramifications. Fig. 59 represents a fragment of this stroma. I regard the double contour which may everywhere be traced at a little distance from the vessels, as the wall of a lymphatic sheath; such perivascular sheaths having been discovered by *Ludwig* and *Tomsa* even in the normal testicle. Here too I had an admirable opportunity of studying the development of vessels from "cœcal protrusions" as described by *Rokitanski;* and I was enabled to assure myself that these protrusions were strictly equivalent to those cœcal appendages of the vascular system with which we became acquainted in connexion with tertiary vascularisation (§ 71). The protrusions, which are undoubtedly cœcal, grow towards each other and coalesce when they come into contact, forming a new capillary loop (fig. 60).

Fig. 59.

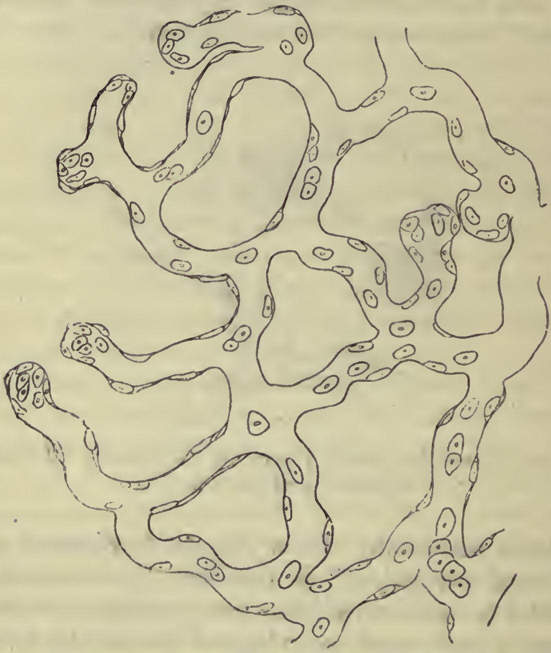


Stroma of a rapidly-growing cancer of the testicle. The section has been pencilled out. $\frac{1}{300}$.

All telengiectatic cancers are clearly recognisable even by the unaided eye, owing to the frequency with which parenchymatous hæmorrhages occur in their interior. Hæmorrhagic foci, varying in size from a pin's head to a hen's egg, and even larger, foci in every stage of retrograde metamorphosis, blood-cysts and patches of pigment of all shapes and sizes, characterise the cut surface of this variety of fungus hæmatodes. As regards malignity, the telengiectatic form of glandular cancer agrees unconditionally with the soft variety.

§ 157. The sarcomatous carcinoma represents the second possible combination of cancer with sarcoma (cf. sarcoma carcinomatodes, § 125). If we imagine the epithelium of an open gland undergoing a degeneration precisely similar to that which gives rise to the soft form of glandular cancer, while the interstitial connective tissue simultaneously undergoes a sarcomatous degeneration, we get a compound tumour, whose place we are at first puzzled to define, uncertain whether to class it with sarcomata or cancers. I place it among the cancers, inasmuch as the sarcomatous element is restricted to the primary growth; when it recurs after extirpation, or forms metastatic deposits, it usually presents the uncomplicated features of soft glandular cancer. Its seats of election are undoubtedly the testicle and the kidney. I venture to assert that most soft cancers of the testicle have a

Fig. 60.



Stroma of a telengiectatic cancer of the testicle, consisting of wide capillaries with cœcal appendages. $\frac{1}{300}$.

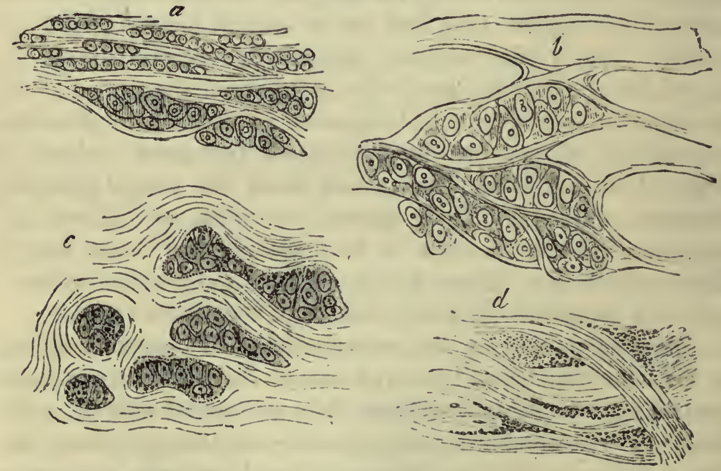
sarcomatous stroma. Its trabeculæ are made up of the characteristic spindle-shaped cells, and are often so thick, that if we purposely take our section from the denser parts of the tumour, we may have to prosecute our search through several times the diameter of the microscopic field, before we come upon a deposit of cancer-cells.

As regards malignity, this tumour also takes its place with soft glandular cancer. It is worth mentioning that it may grow to a colossal size. Kidneys have been met with weighing ten, and testicles weighing fourteen pounds.

§ 158. Hard cancer (simple carcinoma, scirrhus, connective-tissue cancer) differs from the two foregoing varieties by structural and evolutional peculiarities of such moment, that many of my fellow-workers will be most unwilling to admit it to a place among glandular cancers at all. As the epithet I have chosen indicates, it is essentially distinguished from those morbid growths which are akin to it by the greater firmness of its texture. The consistency of a cancer depends on the quantitative ratio between the cellular infiltration on the one hand, and the stroma on the other. Hard cancer owes its greater density to the trabeculæ of its stroma being thicker, and the interstices for the cancer-juice smaller, than they are in the soft form of glandular cancer. And yet its hardness varies within certain limits; its degree being regulated partly by its age and the period of its development, partly by local idiosyncracies. Some hard glandular cancers are of such density throughout that great violence is required to tear them; they creak under the scalpel (durities eburnea; scirrhus). These cancers are white and glistening; the microscope shows them to be made up of a dense, finely-fibrous connective tissue, which contains the nests of cancer-cells in a comparatively small number of fissures and alveoli.

More commonly we find softer and harder portions included in the same tumour, and that in a certain definite order; a hard, central nucleus being enveloped by a peripheral zone of relatively softer—sometimes positively soft—consistency. Examination with the unaided eye alone is enough to make us suspect some connexion between this arrangement and the relative age of the central and peripheral parts. The outermost layer of the tumour (which always occurs in an exquisitely nodular form) consists of a zone of extremely minute, reddish-grey foci, which are embedded in the healthy parenchyma. Next to these come similar foci of progressively increasing size, which ultimately coalesce to form that part of the growth which protrudes like a circular rampart on the surface of section when the tumour is cut across. Farther inwards certain white lines, corresponding to the larger trabeculæ of the cancer-stroma, grow more distinct; the reddish-grey infiltration fades, or is replaced by a yellow marbling, due to the conversion of the cancer-cells into granule-corpuscles (Carcinoma reticulatum of *Müller*). The vessels too of the stroma, which were hardly to be seen in the encircling rampart itself, become much more distinct, mingling red lines and dots with the white trabeculæ of the stroma, and the yellow points of fatty change. Still nearer to the centre these appearances also fade, leaving a white and lustrous hard cicatricial tissue, which sends radiating prolongations from the centre of the tumour towards its circumference. So that, even with the naked eye, we can distinguish four zones which correspond to a like number of stages in the growth of the cancer; a zone of development, a zone of acme, one of degeneration, and one of cicatrisation.

FIG. 61.



Carcinoma simplex mammæ. *a*. Development of nests of cancer-cells; *b*. Fully-developed cancer-tissue (cf. the next); *c*. Commencing cicatrisation; it also represents the relation between stroma and cells in scirrhus; *d*. Cancer-cicatrix. $\frac{1}{300}$.

§ 159. The microscope thoroughly corroborates the evidence of the unaided eye. In fig. 61, the microscopic appearances presented by fine sections taken from each of the four zones of the tumour are shown. Fig. 61, *a*, is from the periphery of a minute nodule, situated in the zone of development; the appearances which it presents used to be interpreted as follows. It was supposed that each row of small round-cells were at once the brood of a single connective-tissue corpuscle which formerly occupied the same point, and the forerunners of a group of cancer-cells, such as might be observed in their immediate neighbourhood. This developmental nexus has now been broken through. The rows of round-cells are viewed as colourless corpuscles which have migrated from the blood-vessels; and great efforts are being made to prove that the nests of cancer-cells originate exclusively from the pre-existing epithelia of the gland-substance. To my mind these efforts appear futile, so far as they are meant to show that all the cancer-cells are actually "descendants" of the epithelial cells. On the other hand I am quite willing to admit that in the hard form of glandular cancer, as in the other varieties, the glandular epithelia undergo fissiparous multiplication, contributing thereby, though only to a moderate extent, towards the enlargement of the acini or tubuli; also, that the first nests of cancer-cells usually originate in immediate proximity to the glandular epithelia, thus giving no little colour to the assumption of an "epithelial infection" of the round-cells which are heaped up in the connective tissue. In my opinion, the development of hard glandular cancer occurs by a slow interstitial inflammation, whose cellular products are converted into epithelial elements instead of pus or connective tissue. The active participation of the glandular epithelia must be regarded as the primary cause of this inflammation, and as the exciting cause of the peculiar line taken by the products of inflammation in their development. Hence the glandular epithelium is and must remain the essential cause of the morbid action, even though its co-operation happen to be quantitatively insignificant. The precise way in which an epithelial direction is given to the development of the infiltrated products of inflammation must for the present be left undecided; although, as has been already hinted, there are many reasons for assuming that young epithelial cells penetrate one by one into the interstices of the adjoining connective tissue, where they infect by contact the indifferent cells which these interstices contain. We are to some extent reminded of the way in which the tegumentary layers of epithelium grow; save that in them the migratory corpuscles of the connective tissue pass over entirely to the side of the epithelium, the boundary line between the epithelium and the connective tissue being thus preserved; while in the present case, the migratory cells are infected while yet embedded in the connective tissue, thereby causing the penetration of the epithelium into the extra-epithelial tissues.

§ 160. Fig. 61, *b*, represents the stage of acme. The proliferated cells demand more space; hence the fibres of the connective tissue are dissociated, and go to form the large and small trabeculæ of a tough stroma; upon and within them ramify the blood-vessels of the cancer, whose calibre and fullness determine the intensity of the red element in the hue of the tumour. That it is fatty degeneration by which the cancer-cells are affected and to which they finally succumb, is clear enough from the mere examination of the juice scraped from a cancerous tumour. In this, all stages of the degenerative process are exhibited side by side (§ 26), from the appearance of the first oil-globule in the protoplasm, to the complete disintegration of the cell. What appear to the naked eye as yellow streaks and dots (carcinoma reticulatum of *Müller*) are found under the microscope to consist mainly of granule-cells. In transverse sections, the thickening of the trabeculæ (of the stroma) which is associated with the diminution in number of the cells, attracts our chief attention. Fig. 61, *c*, represents a type of structure which is permanently characteristic of the so-called scirrhus, but which is met with in every simple cancer as a transitory phase. The trabeculæ are extraordinarily thick; they consist of a connective tissue with short fibres, and provided with spindle-shaped cells. After the total disintegration and removal of the infiltrated cells, this connective tissue has the field to itself. In the cancer-cicatrix, the oldest part of the tumour, we see bands of fibres crossing and inter-penetrating each other in every possible direction; here and there a residue of fatty *débris* indicates the former position of a group of cancer-cells; in other respects, the cancer-cicatrix exhibits no peculiarity which might serve to distinguish it from any other sort of cicatricial tissue (fig. 61, *d*).

The formation of a cicatrix brings the local history of the cancerous tumour to a close; the same termination, when it occurs at the close of a formative inflammation, is known under the name of repair; yet we should not be justified in saying that the cancer underwent "repair" by cicatrisation; for while the reparative process is going on at its centre, new portions of the affected gland are being continually drawn into the vortex of destructive change at the periphery of the growth; so that the cicatrisation always lags far behind the infiltration.

§ 161. Hard glandular cancer occurs most frequently in the female breast, where it presents several varieties; next in order of frequency come the glandular layer of the stomach, the liver and other open glands.

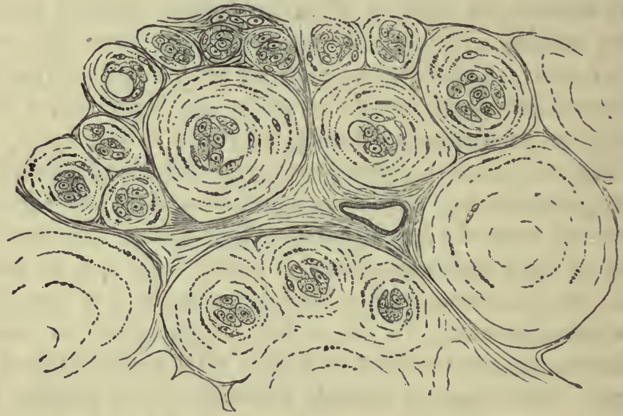
As regards the time at which metastatic deposits begin to appear, nothing is known for certain; as a rule, they occur within a year. Cases are on record of the radical extirpation of hard glandular cancer, not followed by any local return of the disease; but such cases are among the rarest in surgery.

§ 162. Colloid Cancer [carcinoma alveolare, gelatiniform cancer (*Gallertkrebs*)] consists of a soft, tremulous and jelly-like, transparent mass of a bright honey-yellow colour. Essentially a variety of hard glandular cancer, it differs from this, its nearest relative, by the entrance of colloid degeneration into the course of its development. To this colloid degeneration are due the peculiar aspect, the structure and other vital peculiarities of the tumour. First then, as regards structure. The familiar term "alveolar cancer" indicates sufficiently that it is the prototype of an alveolar texture. The stroma is a network with very regular, rounded meshes; and if we inquire into the cause of this striking regularity, we find it in the circumstance that every portion of colloid matter swells, tending, like fluid collected in a limited space, to assume a spherical form; so that any parenchyma which, like this form of cancer, is studded throughout with little portions of colloid matter, must *eo ipso* assume the form of a stroma with spherical meshes.

Having reached a certain size, the colloid spheres by their continued increase in volume, compress the intermediate septa and cause them to waste; two or more spheres coalesce and occupy a space whose original form is slowly obliterated by a gradual levelling of the septa which intersect it, tending to make it assume a spherical shape; so that ultimately a single large, but still globular alveolus is produced. A fine section (fig. 62) shows the entire substance of the tumour to be made up of a number of circular areas, some small, some large, corresponding to the colloid spheres, which are kept apart by septa of connective tissue.

How the colloid matter originates, is a far more difficult question. That it is partly due to retrograde metamorphosis of the cancer-cells, may for the present remain undisputed, since every one of the smaller alveoli is found to contain a group of epithelioid elements, which are no longer to be seen in those of larger size, while there is nothing in their place beyond colloid matter; also, because the colloid metamorphosis described in § 44 may actually be seen to take place in some of the individual cells. But I cannot admit that all the colloid matter present has been generated in this way.

Fig. 62.



Carcinoma gelatinosum. $\frac{1}{300}$.

If we look impartially at the very characteristic appearances presented by colloid cancer (fig. 62) we notice that the groups of cancer-cells contained in the alveoli, are first of all in contact with the alveolar walls; that they are subsequently separated from these walls by a progressively increasing number of layers of colloid matter; and this without their number undergoing either increase or diminution; we notice that they finally become dissolved and disappear after dozens of colloid layers have already accumulated; and a spontaneous conviction arises in our minds, that the major part of this colloid matter has been secreted at the junction of the connective tissue with the epithelium, without the fully-formed epithelial cells taking any active part worth mentioning in the process. The hypothesis of a direct transudation from the blood cannot be entertained for a moment, the endosmotic equivalent of colloid matter being almost *nil.* On the other hand I am inclined to adopt the view put forth by *Doutrelepont* (*Langenbeck's* Archiv, sent in for publication in April 1870), who believes the colloid substance to be a product of the metamorphosis of the material which serves for the construction of epithelial cells, an albuminous compound of some kind, which would, in other forms of cancer, be employed in increasing the number of the cells. We cannot but think in this connexion of *Arnold's* theory of the origin of epithelial cells from amorphous matter; the accumulation of colloid, supposing *Arnold's* view to be correct, admitting of being naturally explained as an accumulation and subsequent transformation of this amorphous plasma. The concentric lamination of the colloid matter points to a certain periodicity in the rate of its secretion, while the fatty and granular *débris* marking out the limits of each layer, will have to be regarded as a bye-product of its manufacture.

§ 163. It is certain that vessels ramify upon the septa and trabeculæ of the stroma in colloid cancer; but these vessels are neither numerous nor large, and contribute but little, even when fully injected, to colour the mass of the tumour, so that colloid cancer always gives one the impression of being very scantily supplied with blood. As regards the course of the disease, and the dangers to which the patient is liable, this circumstance is important, inasmuch as bleeding from the surface of a colloid cancer when broken-up and ulcerating is neither frequent nor abundant.

As regards malignity, colloid cancer occupies a somewhat peculiar position. It has an extraordinary power of infection *per contiguum.* The infiltration of the connective tissue which goes on at its circumference often assumes proportions which are actually colossal. On the other hand, metastases to more remote parts are rare, as also are deposits in the neighbouring lymphatic glands, which for the most part remain unaffected.

Localities: stomach, large intestine, liver, ovary, mammary gland.

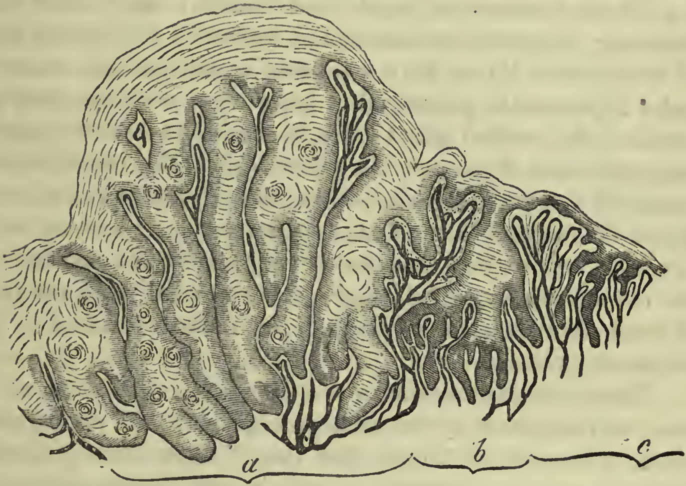
II. EPITHELIAL CARCINOMATA.

§ 164. Were we to take into account every variation in consistency, colour and texture, we should find it difficult to get any two specimens of epithelial cancer, taken from different parts of the cutaneous and mucous systems, which could be viewed as growths of an absolutely identical character; so great is the influence of the parent-soil, especially in the case of epithelial cancer. We must content ourselves for the present with establishing two main categories, corresponding to the two leading forms of epithelium, the *squamous epithelioma* and the *columnar epithelioma.* The former occurs chiefly, but not exclusively, on surfaces clothed with flattened epithelium, the latter on such as are lined with the columnar variety; yet squamous epithelioma is not excluded from mucous membranes clothed with columnar epithelium, *e.g.* the gastric mucous membrane.

§ 165. SQUAMOUS EPITHELIOMA (epithelioma, epidermic cancer, cancroid) forms a white, dense mass of somewhat dry quality, which presents on section either an aspect entirely homogeneous, or affords at most but vague indications of its finer structure. To the finger it imparts a marked sense of resistance, which however is dull and inelastic; on squeezing it forcibly from the side, contorted threads of a milk-white colour protrude from its surface; these have been very aptly compared to the so-called "comedones" which may be squeezed from the sebaceous glands upon the nose. These threads readily break up in water; a cellular emulsion being formed resembling the milky juice of cancer; but the suspended cells are all true specimens of squamous epithelium, indistinguishable from those which line the oral cavity. Certain peculiarities of a minor sort in the form of the individual cells will be more properly discussed when we come to consider the appearances seen in tranverse sections. The nuclei are always of large size, ovoid, double-contoured and furnished with one or more large and lustrous nucleoli.

§ 166. Epitheliomata of the skin and mucous membranes, save when they originate in warts or cauliflower excrescences, (§ 148) always begin as flattened and indurated elevations of the surface. They extend progressively both in depth and in superficial area. Should the growth have reached a certain maximum of development at its place of origin, it breaks open at this point. The surface, somewhat tuberculated from the first, grows rough; erosions, fissures, and holes appear in great numbers, and exude a white, inodorous, pulpy fluid, mixed with pus. The tumour next falls in at its centre; a hollow is produced, which is henceforth masked, either by the dried secretions, or, when these are removed, by the sloughy shreds of the original tissue. In this phase of its development, therefore, the epithelioma presents the appearance of an ulcer with a hard base, and hard, raised edges. At the periphery of the ulcer, we note the constant advance of the infiltration into neighbouring parts; in its indurated border, we can study the characters of its maturity; while towards its

FIG. 63.



Section through the growing edge of an epithelial cancer of the skin. *a.* The fully-developed growth; cylinders of epithelial cells containing pearly nodules (concentric globes), seen in longitudinal section; *b.* An enlarged sebaceous gland; *c.* Commencing elongation of peg-shaped protrusions of the epidermis in an inward direction. $\frac{1}{150}$.

centre, we mark the disintegration of the morbid growth, and the phenomena of repair, which are occasionally very distinct.

In considering the development of this variety of cancer, it is convenient to distinguish between its first beginnings and its subsequent extension. Thin vertical sections through the raised border of an epithelioma of the skin, are best adapted for the more accurate determination of its point of origin (fig. 63.) Proceeding from without inwards in our examination of this section, from *c* to *a*, the first indication we have of the beginnings of the morbid growth, is a striking enlargement of the sebaceous glands (*c*). These increase in length and breadth; their cæcal ends becoming irregularly nodulated and clubbed. At the very edge of the tumour (*b*) we have a colossal example of this change; and a dispassionate investigation leads us to conclude that the tubuli of the swollen gland differ in no respect from the adjoining protrusions of the cancroid growth (*a*). This resemblance is especially due to the fact that during the elongation and thickening of the fundus of the gland, its character as a secreting organ is wholly lost; we miss the central cavity and the oil-globules; we can see nothing but closely aggregated epithelial cells, and these of such dimensions as far exceed the normal standard of the sebaceous epithelia.

These considerations make it credible that epithelioma of the skin may originate in the sebaceous glands; but on the other hand, we must not forget that this "origin from sebaceous glands" must be regarded as only a part of the entire phenomenon, which consists in *a thorough dislocation of the boundary-line* (Grenzverrückung) *between epithelium and connective tissue.* On the one hand, we owe to *Thiersch*[*] the account of an epithelioma which sprang demonstrably from the sudoriparous glands; on the other, we may see in any and every epithelioma, that it is not the glands alone which take part in the formation of the cancroid protrusions. Club-shaped processes of epithelium burrow into the underlying tissues from the deepest points of the epithelial stratum, from those convexities of the rete Malpighii which lie in the inter-papillary furrows; and it is this phenomenon, to which the elongation of the *existing* epithelial protrusions (*i.e.* the glands) is quite subordinate, which stamps a common character on every variety of primary epitheliomatous growth.* It is not therefore as glands, but as appendages of the epidermis, that the sebaceous and sudoriparous follicles take part in the proliferation. They lose their glandular character and are converted into what they originally were, solid aggregates of cells, forming peg-shaped appendages of the under surface of the epidermis.

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[*] *Thiersch,* Der Epithelialkrebs. Leipzig, Engelmann, 1865.

§ 167. Opinions differ concerning the way in which the epithelial sprouts grow and penetrate into the sub-epidermic layer of connective tissue. According to *Thiersch*, *Billroth* and others, the sprouts grow exclusively by proliferation of their epithelial elements; *Köster* holds that their increase is additive, and due to a corresponding metamorphosis of the endothelial cells of the lymphatics, in whose interior the sprouts exclusively extend. For my own part, I cannot overlook the very striking fact, that active fission of cells and nuclei may be seen to take place in the sprouts themselves; neither can I ignore the eloquent appearances exhibited by sections taken from the raised border of certain flat epitheliomata in a direction parallel to their surface, as *Köster* recommends.

Fig. 64 exhibits the superficial lymphatic network of the cutis in its highly characteristic configuration, but with its interior occupied by cylindrical masses of epithelial cells. The lymphatics in this specimen are undoubtedly the channels along which the epithelial sprouts advance. It must not be inferred from this, that they perform a like office in the case of *all* cancers; indeed we may find it necessary to admit that the interesting appearances discovered by *Köster* are only the microscopical expression of a fact already known, *sc.* that cancers and sarcomata of glandular organs (*e.g.* of the kidney, the testicle, the lymphatic glands) are especially prone to penetrate into the interior of the blood-vessels and lymphatics, in which they subsequently extend. Whatever be our conclusion, the observation itself is a reliable one, and sheds much light on the way in which certain kinds of cancer penetrate into and extend through the parenchyma of organs. With this part of *Köster's* theory, the independent growth of the epithelial sprouts asserted to take place by *Thiersch* may very well be reconciled. It is only the additive growth by metamorphosis of the lymphatic endothelia, which is radically incompatible with *Thiersch's* views. I have always warned my hearers against the danger of adopting a one-sided conclusion on this matter, and I do not even now see any reason for deserting the *via media* which I have hitherto followed. In epithelium (as *e.g.* also in cartilage) I distinguish between a primary and a secondary mode of growth; the former consisting in the addition of young and small cells at the junction of the epithelium with the connective tissue, the latter in an enlargement and proliferation of the cells in the middle of the epithelial layer. To the former of these two factors is due the growth in length and breadth, to the latter the sudden condensation of the young stratum which is familiar to every microscopist. (Cf. the skinning over of raw surfaces, fig. 39). The phenomena are the same in disease. The actual extension of the epithelial sprouts is due to the apposition of mobile cells derived from the nutrient apparatus (according to *Köster* of proliferated endothelia) to their most advanced points. Their subsequent

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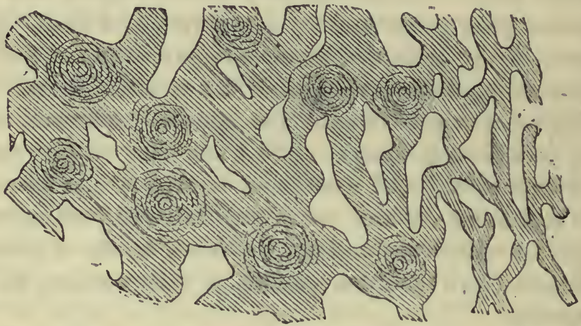
* From an examination of epitheliomata of the digestive tract, I have come to the conclusion, that the tubular glands of the mucous membrane, lined with columnar epithelium, play the same part as the sebaceous glands of the skin. They extend inwards, and change their character, losing their central cavity, and forming solid aggregates of cells; these aggregates consisting first of indifferent elements, subsequently of true squamous epithelia.

FIG. 64.

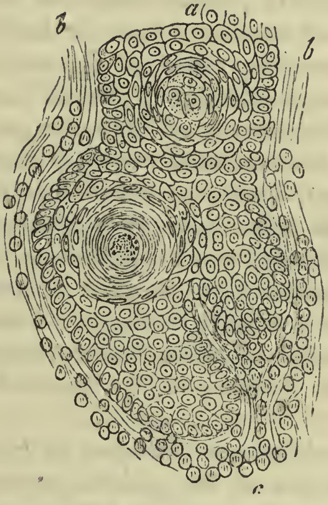


Horizontal section through the proliferating zone of an epithelial cancer of the skin. Extension of the epithelial protrusions along the interior of the lymphatic vessels. After *Köster*.

condensation and conversion into tough, peg-shaped processes of epithelium, is in great measure a result of cell-proliferation in the axis of the sprouts themselves.

§ 168. Passing on to consider the *structure* of the tumour, (fig. 63*a*) we see at a glance that it is chiefly made up of the epithelial cylinders already alluded to as "peg-shaped protrusions." The average diameter of these cylinders is one-seventh of a line; their length is usually very considerable, though it is not often that we have an opportunity of seeing the whole of any one cylinder. They bifurcate, sometimes repeatedly, forming perfectly dendritic structures. The arrangement of the epithelial cells, as seen in transverse sections, is highly characteristic. At the junction of the epithelium with the connective tissue, at the periphery therefore of the protrusions, a layer of small, roundly-oval elements, often of a brownish tint, is found; this intervenes between the connective tissue on the outside, and the more

Fig. 65.



Section of an epithelial cylinder under a magnifying power of 500 diameters. *a*. The cylinder itself, exhibiting the characteristic stratification of its cells, and two pearly nodules, one of which is older than the other; *b*. The stroma; at *c* it contains a very large proportion of corpuscular elements and contributes directly to the additive enlargement of the cylinder.

highly-developed squamous elements interiorly (just as in the healthy cutis). These small cells fill up all crevices; everything is continuous, there are no breaks. And a tendency to *concentric lamination* prevails throughout.

We may fairly assume that inasmuch as the infiltrated parenchyma is not capable of being stretched beyond a certain point, the peg-shaped protrusions cannot attain more than a certain definite thickness. Now supposing that new cells continue to be formed it is clear that the available space must sooner or later be exhausted; pressure must arise in the interior of the tumour, which will be exerted both on the processes themselves and on the connective tissue of the intervening stroma. I regard this "compression due to growth" as a very important element in the life-history of all infiltrative growths; for, in so far as it compresses the interstitial vessels, it must hinder the circulation of the blood, disturb the nutrition of the parts, and thus, as a rule, be the prime cause of degenerative changes. This part of its action is the same in epithelioma as in other tumours; I am inclined moreover to assign it a share in the tendency towards lamination alluded to above, a tendency shown by the cells in the interior of the epithelial protrusions, and which culminates in the formation of the so-called "pearly globes or nodules."

The pearly globes are produced as follows (fig. 63): at intervals in the axis of the epithelial protrusions, one or two cells which retain their spherical form, serve as a nucleus to which the adjacent elements are applied like the concentric scales of a bulb; these elements being flattened out, so as to yield the optical effect of fine dark lines when seen edgeways, just as in the hairs and nails. Large numbers of cells are thus squeezed into a small, globular space; the entire mass presenting a homogeneous, intensely yellow and lustrous aspect, which recalls the colour of hair. The individual nodules may grow to a considerable size; and we shall find in what is known as "pearly cancer" (*see* cysts of nervous organs, brain) a form of epithelioma in which the entire tumour is ultimately converted into an aggregate of pearly nodules.

The cells of epithelioma are also liable to another interesting change, which is not, however, common; they may become grooved. This term is applied to cells whose surface is beset with a large number of parallel ridges, only visible under high powers; these ridges being suturally adapted to the corresponding grooves or furrows of adjacent cells, thereby causing an exceedingly firm union of the cells among themselves.

§ 169. The second constant element in the structure of epitheliomata is a stroma made up of connective tissue. Inasmuch as the bodies with which it shares the space assigned to the entire tumour are of a cylindrical form, it must needs constitute a honeycomb-like framework, the open ends of the cells being directed outwards. The stroma consists at first of the parenchyma of the cutis or mucous membrane dislocated and frayed out. We learned on a former occasion (§ 83) to regard the epithelium, apart from its first differentiation in the embryo, as in every case a product of the connective tissue; hence we may take it for granted that the stroma plays a very active part in epitheliomatous growth. We actually find, especially at those points where the growth of the epithelial protrusions is most active, that their apices are tipped with a luxuriant proliferation of cells (*c*); the stroma is richly provided throughout with young elements; moreover it is prone to take on an independent activity, which usually leads to the development of papillary excrescences.

The stroma carries the vessels of the tumour; they share its fate in all respects; when the stroma wastes, they are obliterated; when it developes a productive activity, they dilate (*see* below). Fig. 63 shows a successful injection of the vessels, executed according to the directions given by *Thiersch.*

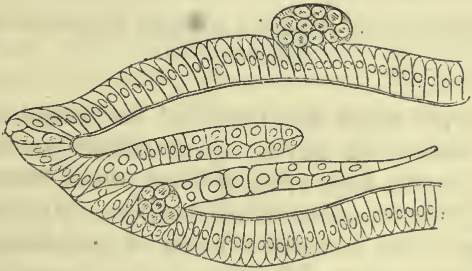
§ 170. We come now to the degeneration of epithelial cancer. Its conditions are involved in the growth of the tumour itself. Attention has already been called to the possibility of the "pressure due to growth" interfering with the circulation, and so disturbing nutrition in larger or smaller sections of the tumour. These disturbances are first felt as a rule in such points of the tumour as are already subjected to unfavourable nutritive conditions. Such points are the centres of the epithelial protrusions. The thicker the protrusions, the farther their axial cells are from the soil which gave them birth and which should nourish them. The circumstance that these are the first-formed and consequently the oldest cells operates in the same direction; so that we usually find the phenomena of retrograde metamorphosis beginning in the axis of the protrusions. The phenomena in question consist mainly in fatty degeneration of the epithelial cells, leading to the formation of a number of atheromatous abscesses. These are originally distinct, but they gradually coalesce to form a single cavity extending through the entire length of the protrusion. Such cavities may be recognised on the surface of the epithelioma even with the naked eye as yellowish-white, comedo-like points. They ultimately burst; the excavated protrusions open up and discharge their contents on the surface. The tumour thereupon collapses, and the ulceration, the discharge of pus and atheromatous pulp, to which allusion has been already made, begins.

Epithelioma does not belong to the most malignant group of morbid growths. At least cases of radical extirpation (*i.e.* with no attempt to spare surrounding parts) not followed by any return of the disease, have been vouched for by responsible observers. Such cases, indeed, are by no means common. Within a year from the operation, the cicatrix generally becomes the seat of a new growth of analogous character. On the other hand, metastasis proper is comparatively rare. The nearest lymphatic glands are the first to be affected; the internal organs not being involved until the primary mischief has attained dimensions so colossal, that the trifling metastatic lesions are unimportant in comparison. The metastasis is probably due in all cases to the immigration of young epithelial cells, which cause an "epithelial infection" of the autochthonous elements of the conjoint vascular and connective-tissue system at the point where they settle.

§ 171. Columnar Epithelioma. Until very lately, observers could not agree whether to regard the crypts of *Lieberkühn* in the digestive tract as genuine tubular glands, or merely as crypts, *i.e.* cæcal inflexions of the surface solely designed to increase its superficial area. The difficulty was mainly histological; for it was shown that these so-called glands were lined throughout with columnar epithelium of exactly the same kind as that which clothed the free surface itself and its papillæ. The results of pathological histology are not in any way adapted to allay the scruples thus aroused; for the only affection from which we might expect to gain some conclusive evidence on this subject, *sc.* columnar epithelioma of the digestive tract, involves the epithelium of the crypts and that of the papillæ in so uniform a manner, exhibits so constant a ratio between the elevations and depressions of the dermo-epithelial boundary-line, that it is absolutely impracticable to draw a hard and fast line between the two. This explains how it is that the very same morbid growth may, with equal fairness, be regarded as a destructive papilloma (*Förster*), or a proliferating adenoma (*Klebs*).

To these two observers we owe what knowledge we possess concerning the finer details of the development of columnar epithelioma. The alteration invariably begins with a deepening of the glandular tubuli and an increase in the number of their terminal divisions. Here, however, it is important to note that this phenomenon from the very first, I feel almost inclined to add, designedly, presents the character of an extension of superficial area; for we never find *solid* cellular protrusions like those in squamous epithelioma, but always protrusions of the existing cavity of the gland, which are lined with a single layer of columnar cells. The growth next proceeds to cause a *positive* extension of surface; *i.e.* to produce papillary excrescences from the walls of the cavities. In this connexion, some statements made by *Klebs* are of great interest; he says that acuminated and club-shaped outgrowths, consisting at first entirely of epithelial cells, rise from the fundus of the glandular tubuli (fig 66). At a later period we find branching papillæ, which grow in all directions, and especially inwards, contributing thereby to the destruction of the affected parts.

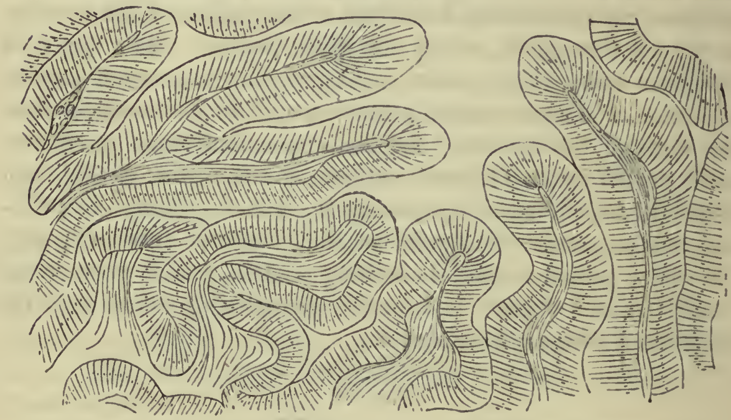
Fig. 66.



From an adenoma of the digestive tract. Copied from *Klebs*. (Handbuch der Patholog. Anatomie, fig. 4.)

The free surface of the mucous membrane has already begun to take part in the process by a more or less exuberant proliferation of papillæ. The free surface however is to be regarded generally as a *locus minoris resistentiæ*; accordingly the tumour as a whole projects above it, first as a flat and uniform, later as a fungoid elevation. To enable us justly to appreciate its complicated structure, and more particularly to discriminate between the papillary outgrowths and the inter-follicular septa, which are likewise coated with columnar epithelium, we must make use of specimens teased out with needles, or sections of a certain thickness; since, in very fine sections, there is no break in the continuity of the outline which passes from elevation to depression and *vice versâ*, without indicating the concavity or the convexity of the epithelial ridges (fig. 67).

FIG. 67.



Vertical section through a columnar epithelioma of the stomach. $\frac{1}{300}$.

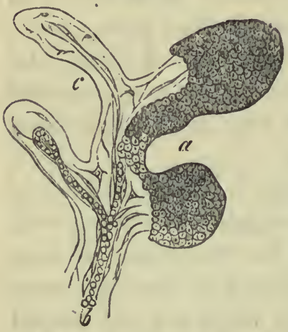
§ 172. I am aware that nearly all the mucous membranes, especially those of the larynx, uterus, bladder and others, have each their peculiar form of epithelioma, which differs from the chief types, from the squamous and columnar epitheliomata, in the same degree as the transitional forms of epithelium with which these parts are clothed, differ from the simple squamous epithelium of the skin, or the simple columnar epithelium of the stomach and bowel. For a detailed account of these finer variations I refer the reader to the special division of this work.

Cylindroma (Appendix).

§ 173. The question concerning the essential character of a tumour, termed by *Henle* siphonoma, by *Billroth* cylindroma, by *Meckel* tubular enchondroma, by *Friedreich* tubular sarcoma, by *Förster* and its most recent investigator *Köster* mucous cancroid, presents itself among all discussions concerning the fundamental nature of cancer and sarcoma, as an enigma of equal interest and difficulty which chance has thrown in the way, now of one, now of another inquirer. The number of names which have been applied to this growth, show clearly enough that the different observers differ widely in their views concerning it. Are we justified in assuming that all the cases which have been examined are really identical? In favour of this assumption we have the fact of their common situation in the region of the face, particularly in the orbit and surrounding parts; while the circumstance that the earlier observers devoted their chief attention to the most singular and not to the most essential constituents of the growth, may go some way towards explaining and excusing their differences of opinion.

Those singular constituents are certain "hyaline bodies" of considerable size, which may readily be isolated by teazing with needles. We are struck first of all with the strangeness of their outward form. Together with perfect spheres, we find specimens of a more cylindrical shape; others again which are club-shaped and cactiform. The hyaline chains often seem to diverge from a common centre. I cannot now review the manifold hypotheses concerning the mode of origin and farther development of these bodies, hypotheses in which the prevalent histogenetic theories are for the most part mirrored. I will only say that *Billroth's* view, according to which they are perivascular sheaths of mucous tissue or fragments of such sheaths was the most generally adopted one, until *Köster* recently showed, from a very careful study of the development of the tumour as a whole, that the hyaline globes, cylinders, &c., were the product of a secondary, hyaline metamorphosis of the cellular trabeculæ of a cancroid growth of the lymphatic vessels. He believes that we have to do in all cases with a cancroid proliferation of cells taking place in the lymphatic networks of the affected part. The endothelia of the lymphatics proliferate; the canals are blocked by cellular cords resulting from their proliferation; and the cords naturally ramify and anastomose with one another like the lymphatics themselves. Thereupon, the hyaline degeneration sets in, beginning in the axis of the cords. It may even be demonstrated in individual cells; at a later period, however, the products of degeneration coalesce to form those larger globes and cylinders whose original cellular composition is at best but faintly indicated by the presence and stellate arrangement of a finely-granular material coinciding with the intercellular limits. The hyaline degeneration may implicate the whole of the epithelial coat, a hyaline cylinder of relatively large size appearing to be embedded in the connective tissue of the stroma.

Fig. 68.



Cylindroma from the cortex cerebelli.

The presence of blood-vessels in the axis of the hyaline cylinders, which I have succeeded in demonstrating in a tumour extending to the cerebral substance (fig. 68), is explained by *Köster* by the well-known perivascular disposition of the lymphatic sinuses.

Cylindroma is very liable to recur after removal, but it seldom gives rise to metastatic deposits; accordingly it deserves a place near the carcinomata. To distinguish it from the glandular and epithelial forms of cancer, it may be allowed to retain the name of cancroid, which used formerly to be applied to all the varieties of epithelial cancer indiscriminately.

SPECIAL PART.

I.—MORBID STATES OF THE BLOOD AND THE ORGANS CONCERNED IN ITS RENEWAL, PARTICULARLY THE SPLEEN AND LYMPHATIC GLANDS.

a. DYSCRASIÆ.

§ 174. The blood plays such a weighty part in pathology that it seems necessary to explain why so little space will be devoted to a consideration of its morbid states in the present manual.

The position of the blood in the domain of pathology is determined by its physiological significance. The blood is the medium through which the interchange of matter in the organism (Stoffwechsel) is carried on. It is the nutrient fluid, which supplies each individual part of the body with the pabulum indispensable for its existence; it removes the effete and hurtful products of the chemical processes associated with nutrition, and carries them to the excretory organs for elimination. Viewed in this light, the blood is the meeting-place of divers chemical compounds, some of which have already taken part in tissue-metamorphosis, while others are about to take part in it; of compounds whose presence in the blood is in every case only *temporary*, and which thus give to the blood itself a certain variability of chemical composition, for which not the blood but the organs of the body are really answerable.

Even if we view the blood as an organ, it is peculiarly liable to change in comparison with other organs. Our right to call the blood an organ cannot be disputed. For it has an independent origin from embryonic tissue in the *area vasculosa*, apart from other organs; it possesses specific cells—the blood-corpuscles, which subserve a specific function—that of fixing the oxygen of the air. We must not allow ourselves to be led astray by the fact that the corpuscular elements are separated by a fluid intercellular substance—that the blood itself is a fluid. Its structural elements are themselves of very unstable character. The blood is rightly held to be that tissue whose losses are soonest remedied, whose morphological and chemical constituents undergo on the whole the most rapid change. We must recollect moreover, that it does not elaborate its constituent elements within itself, but draws its supply of cells from the lymphatic glands, the spleen, and according to *Bizzozero*, *Neumann*, and others, from the marrow of bone, and its albumen from the alimentary canal. In this respect too therefore, certain determinate organs are responsible for the composition of the blood. Accordingly the blood is kept in its normal state by the systematic co-operation of several factors; by the due admixture and transformation of its histogenetic elements; by the uniform and easy supply and removal of the more transitory nutrient and excrementitious substances; finally by the rigid exclusion of abnormal or injurious matters from whatever source. Any irregularity in these conditions alters the composition of the blood, and gives rise to a *dyscrasia;* and indeed, the vast majority of blood-diseases are nothing more than such morbid alterations of its composition.

§ 175. But few of the manifold dyscrasiæ of the blood admit of being investigated anatomically; only those indeed which depend upon morbid changes in the visible elements which are suspended in the colourless liquor sanguinis. These elements are usually distinguished as:

1. The red blood-corpuscles; flattened, biconcave discs, about four times as broad as they are thick, without nuclei, without a cell-membrane (?), made up of a colourless protoplasm (stroma), and a reddish-yellow fluid material (hæmato-crystallin).*

2. The colourless blood-corpuscles or leucocytes, which are so rare in healthy human blood that for every 450 red corpuscles we find only one white one. These cells are destitute of

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* Besides the discoidal blood corpuscles we always find a certain number which have become spherical. These are characterised by their apparent smallness, and their darker, almost reddish-brown hue, peculiarities readily explained by supposing that the same quantity of matter which was previously spread out into a shallow disc, has shrunk together to form a sphere.

a limitary membrane; they are made up of a finely granular protoplasm containing distinct nuclear structures. We find either a single, round nucleus of considerable size, or from two to five smaller ones of lustrous aspect. In form the white corpuscles vary, inasmuch as they are endowed with a high degree of spontaneous contractility; in dead blood, they are spherical. Accordingly they are cells, which resemble in every respect the corpuscular elements of embryonic tissue and of pus, from which indeed they can hardly be distinguished by any anatomical criteria.

3. The elementary vesicles discovered by *Zimmermann*, circular, colourless bodies with indistinct outlines, which owing to their small size and transparency are only to be detected under very high powers, but which are occasionally present in enormous numbers.

1. *Chlorosis.*

§ 176. The chlorotic dyscrasia is essentially characterised by a falling-off in the number of *all* the above-named structures. Of all alike, so that the proportion of the red to the colourless corpuscles is in no wise altered. The blood as a whole seems thinner and more clear—one might almost say more watery than usual; on evaporation, the percentage amount of solid residue is decidedly below the normal average; all this however is due, not to any increase in the amount of water, but to a positive diminution in the number of cells. Where an organ depends for its colour on the blood it contains, as *e.g.* the mucous membranes (conjunctiva) and certain parts of the skin—we observe a peculiar paleness, which has caused the name of "green-sickness" to be given to the disease.

The etiology of chlorosis is still involved in some doubt. So much is certain, that the chlorotic dyscrasia does not depend upon a premature destruction, upon an atrophy of blood-corpuscles, but upon an inadequate supply of young and vigorous elements to take the place of those which have completed their term of existence, and are only fit to be cast out. But beyond this, we cannot tell whether a functional disturbance of the organs of sanguification (the spleen and lymphatic glands) or some disorder of the more remote factors in the process (*e.g.* chylification) is to blame. *Virchow's* view is deserving of especial notice; he finds that the aplastic state of the blood is associated with a certain aplastic condition of the circulatory apparatus as a whole, *sc.* the heart and arterial system (*see* below), so that chlorosis would have to be viewed as a congenital, and not, as is generally held, an acquired disease.

2. *Leukhæmia.*

§ 177. The leukhæmic dyscrasia depends upon an alteration in the numerical proportion of the white to the red blood-corpuscles. We have already given 1 to 450 as the average ratio of white to red corpuscles. A moderate increase in the number of the colourless cells is consistent with health and may be demonstrated *e.g.* after every full meal. But if the number of the white corpuscles undergoes so marked an increase in proportion to that of the red ones, that we find *e.g.* one white to ten red elements, or even an equal number of both, then indeed the condition becomes manifest even to the unaided eye as a decolorisation of the blood; the blood assumes a paler, raspberry-like hue, and we are thus entitled to speak of "white blood" or leukhæmia. This most interesting morbid state was described in 1845 by *Virchow* and *Bennett* simultaneously; the German pathologist however deserves the credit of having from the first recognised and explained its real meaning. According to him, we have to do with an increased supply of colourless corpuscles to the blood, due to a morbid state of those very organs which normally supply the blood with its colourless elements, viz. the spleen and the lymphatic glands.

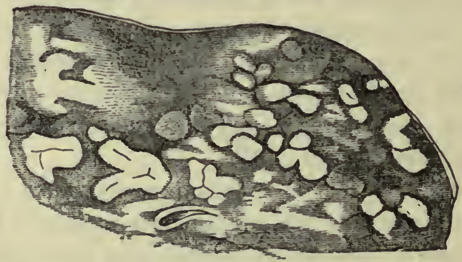
§ 178. The SPLEEN has long been held to play an important part in the renewal of the blood; in our time it has been regarded, now as the grave of the red corpuscles, now as the birthplace of the white ones; *Kölliker* has justly attributed both of these functions to it. The excess of colourless cells in the blood of the splenic vein is an indisputable fact; they are from five to ten times as numerous as in arterial blood. It is equally certain that the lymphatic glands, particularly those of the mesentery, are a source of white corpuscles. If we compare the lymph of the thoracic duct with that of the peripheral lymphatics before they enter the glands, we find that the former contains a far larger proportion of lymph-corpuscles. The afflux of leucocytes from the spleen and lymphatic glands is not uniformly rapid at all times. It is most active a short while after meals. This increased activity coincides with that transient hyperæmia of the entire digestive tract which is caused by taking food, and which manifests itself in the spleen more especially as a perceptible intumescence of that organ. If we have the chance of examining a spleen under such circumstances, we find, besides a marked congestion of its pulp, a distinctly swollen condition of the Malpighian bodies. The mesenteric glands too are larger and contain more blood than usual. It is probable therefore that the increased supply of blood occasions a more rapid production of leucocytes in the Malpighian bodies of the spleen and in the mesenteric glands. The newly-formed cells mingle with the current of lymph or of blood as the case may be, and a transient leucocytosis is the result; no sooner however does the digestive hyperæmia of the abdominal viscera subside, than the lymphatic organs on the one hand, and the composition of the blood on the other, return to their normal state.

§ 179. Leukhæmia too is commonly associated with an enlargement of the lymphatic organs. The spleen here takes the lead. By far the greater half of all leukhæmiæ are purely splenic; more rarely do we find the lymphatic glands diseased together with the spleen; and an exclusive affection of the lymphatic glands is rarest of all.

The *leukhæmic spleen* is originally a congested spleen. The blood, flowing more slowly, accumulates mainly in those anastomotic channels of the pulp, which were first recognised by *Billroth* as a part of the blood-path through the spleen, and termed " cavernous veins " on account of their easily demonstrable connexion with the efferent vessels. The lymphoid parenchyma of the pulp (the intervascular cords of *Billroth*) is also involved in the process; in addition to the usual colourless cells of the spleen we find an unusual number of red corpuscles; the Malpighian bodies too are enlarged, though the alteration in *their* structure is not as yet very striking. With the naked eye, besides the dark colour, diminished consistency, and increased volume of the pulp, we perceive a distinctly lobed or rather tuberous condition of the surface of the organ. Each of these elevations corresponds to the area of distribution of a splenic arteriole (*penicillus*), while the intervening depressions coincide with the insertion of the larger trabeculæ, these taking a longer time to accommodate themselves to the enlargement of the organ as a whole. The capsule too does not admit of any very sudden distension. In my notes of *Virchow's* practical course (Berlin, 1857-58) I find a case of splenic leukhæmia in which the spleen (in the stage of parenchymatous congestion) was swollen till it measured one foot in length, two inches in thickness, and five inches in width; and in consequence of this, a rupture of the capsule had occurred. The fissure, masked by clotted blood, was three lines in length, and passed at each end into a commencing dissociation of the capsular fibres, preliminary to an extension of the tear.

§ 180. As the disease advances, an overgrowth (hyperplasia) of the Malpighian bodies—or as we must call them nowadays, the lymphoid sheaths of the arteries—developes itself more and more. The first step in the process is an accumulation of leucocytes in their interior, produced by fission of those already present. This proliferation is followed by a dilatation of the delicate fibrous reticulum between the cells, and subsequently by a proportionate formation of new capillaries, so that the enlargement of the Malpighian bodies really implicates every one of their three constituents, and must therefore be regarded as a true overgrowth. The Malpighian bodies are now very distinct on the cut surface of the spleen as white, tough, resistant nodules; they exhibit, more often than under normal conditions, a tendency to bifurcate, nay even to break up into a number of branches, a proof that they have not only increased

FIG. 69.



Cut surface of spleen in the second stage of leukhæmic swelling. Enlargement of Malpighian bodies. Atrophy with pigmentation of the pulp.

in thickness, but have also extended either upwards or downwards along the vessels to which they are attached (fig. 69).

The overgrowth of the Malpighian bodies naturally contributes a new element to the existing causes of splenic enlargement. The spleen attains the greatest length, breadth, and thickness of which it is susceptible. Inasmuch however as the morbid phenomena must run their course in a space limited by the size of the splenic capsule, it is self-evident that degenerative changes must coincide with the hyperplastic processes in order to make room for the latter. The former chiefly affect the pulp, which, wedged in between the continually growing Malpighian bodies, perishes in large portions at a time. This is always associated with an abundant production of pigment, which reaches its maximum in the immediate neighbourhood of the glistening Malpighian bodies, giving rise to an exceedingly variegated "granitic" marbling of the cut surface. The consistency of the organ conforms to that of its chief constituents, the Malpighian bodies; it becomes peculiarly tough, more than leathery, almost wooden. In addition to all this, we have chronic inflammatory changes in the peritoneal coat which give rise either to smooth or reticulated thickenings of cartilaginous hardness, or else to highly vascular membranous adhesions connecting the spleen with the nearest abdominal viscera.

§ 181. With splenic leukhæmia *Virchow* contrasts that rarer form to which he gives the name of *lymphatic leukhæmia;* it is characterised from the first by the predominant way in which the lymphatic glands are affected, while the splenic tumour is either secondary or altogether absent. The glands do not all swell at once; the disease usually begins in an inguinal or axillary gland and spreads first to all the glands in the same region; it then extends inwards in the direction of the thoracic duct, involving the mediastinal or retroperitoneal groups of glands; then other peripheral glands take on the morbid action, until every lymphatic gland in the body is more or less enlarged. The individual glands often attain from three to five times, occasionally even ten times their natural size. Nevertheless, an anatomical investigation shows nothing beyond a simple overgrowth in every case. This indeed is clear enough from the fact that even in cases of extreme enlargement the lymph-paths remain open, and the lymphatic sinuses of the gland can be injected both from the afferent lymphatics, and by direct puncture. An examination of thin sections which have been pencilled out shows nothing which might not occur in a normal gland; fine-meshed reticulum made up of thin, lustrous threads, permeated by capillaries and occupied by lymph-corpuscles. We notice only that the cortical nodules (Rindenknoten) and the medullary cords (Markstränge) are far broader, and the capsules and septa of connective tissue far thicker than they usually are. *W. Müller* asserts that in hyperplastic enlargements of the lymphatic glands the delicate network of connective-tissue corpuscles which permeates the lymphatic sinuses of the cortex and the lymph-paths of the medullary substance, shows itself to be the essential histioplastic element, inasmuch as new layers of medullary substance, in addition to those already present, are more particularly developed in its neighbourhood. I believe that this is principally true of leukhæmic overgrowths. (*See* below.)

§ 182. The pathological histology of leukhæmia is not exhausted with the consideration of these hyperplastic conditions of the spleen and lymphatic glands. The implication of other organs suggests that we ought rather to view those phenomena merely as the expression of a general tendency to the development of new lymphadenoid tissue. The presence of a certain quantity of unformed connective tissue seems in fact to be the only condition needful for the occurrence of the characteristic alterations. The cells proliferate, and form circumscribed deposits of variable size, which are white to the naked eye, and which can only be distinguished from small collections of pus by the circumstance that the cells are embedded in a network of delicate fibres of stiffened protoplasm, which leaves enough space round the cells for the transit of nutrient fluid. It need hardly be said however, that this very reticulum in which the cells are embedded, and which distinguishes the leukhæmic product from a collection of pus, assimilates it to the lymphatic glands, raises it to the level of lymphadenoid tissue. (Cf. leukhæmic swelling of the liver, kidneys and serous membranes in the corresponding chapters of the Special Part of this work.)

3. *Melanæmia.*

§ 183. In the melanæmic dyscrasia, certain pigmentary particles are found among the usual floating constituents of the blood; in well-marked cases, they occur in every specimen of blood taken from the heart's cavities. Their shape is very irregular; they are made up of yellow, brown, but most commonly of black granules; most of them are small, smaller at least than red blood-corpuscles; others are larger, and a few even exceed the red corpuscles considerably in size.

Here and there we may succeed in demonstrating a transparent, colourless membrane investing the pigmentary aggregates and filling up the irregularities of their surface. In rare instances, this membrane is of considerable thickness, and then exhibits a concentric lamination.

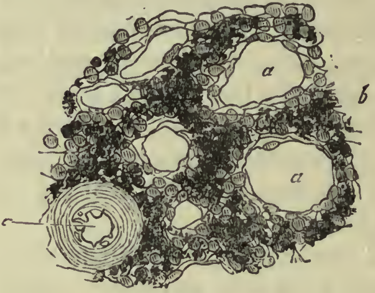
§ 184. In the General Part of this work I spoke at length about the mode in which pathological pigments originate. The remarks I then made are perfectly applicable to the pigmentary particles of melanæmia. They are derived from the colouring-matter of the blood, and consist of condensed and altered hæmatin precipitated in a granular form. Both the circumstances and the locality of their production may be determined with some approach to certainty. Melanæmic pigment originates chiefly in the spleen, under the influence of the malarial cachexia (cachexia of intermittent fever).

The morbid anatomy of intermittent fever starts from an active congestion of the liver and spleen. Both of these organs may attain a very considerable size in consequence. Nevertheless, it is only after the hyperæmia has lasted some time that signs of permanent disorganisation occur. One of these, a diffuse interstitial overgrowth of connective tissue, we shall become acquainted with among the diseases of the liver as an induration of that organ. The spleen may either exhibit a kind of softening of its entire parenchyma, or an indurative condition which starts from a thickening of its capsule and trabecular network. In very severe cases, such as (thanks to the general use of Peruvian bark) only occur sporadically in Germany, this is associated with a deposit of pigment both in the liver and in the spleen.

This is directly traceable to the above-mentioned excessive and prolonged congestion of both organs. In the liver, the pigment makes its appearance just outside the vessels; numberless minute extravasations into the capsule of *Glisson* and the hepatic parenchyma form the starting-point of the process. In the spleen, whose peculiar structure excludes the possibility of extravasation, since the blood could only be extravasated out of one of its natural channels into another, the pigmentation occurs in the intervascular cords of the pulp—in those parts therefore where the blood flows most slowly. Even under normal conditions we may here observe the development of pigment-cells and blood-corpuscle-holding cells (cf. note to § 57). In the pigmented spleen the intervascular cords are so thickly packed with the black, flaky masses (fig. 70, *b*) that the organ presents even to the naked eye a colour varying from slate-grey to black (the *milza nera* of the malarious districts of Italy).

From hence the pigment-flakes make their way into the blood. We know that the intervascular cords are not shut off from the cavernous veins by an impermeable membrane (fig. 70, *a*); we regard the former in the light of a filter with very fine pores intercalated between the arterioles on the one hand, and the venous radicles on the other, and which, in the spleen, takes the part of the capillary vessels and parenchyma of other organs. During this filtration the pigment-flakes are torn from their place of origin and pass into the blood, where their presence gives rise to the melanmiæc dyscrasia. The black particles are accordingly carried wherever the blood itself penetrates. We find them in all the organs of the body, especially in those which are characterised by the narrowness of their capillaries, *e.g.* in the brain. All the flakes cannot pass through this

FIG. 70.



The melanæmic spleen. Transverse section from the middle of the organ. *a.* The cavernous veins of the spleen; *b.* The intervascular cords containing pigment; *c.* A branch of the splenic artery. $\frac{1}{300}$.

organ; the larger ones are arrested *in transitu.* The vessels give way behind the point of obstruction; hæmorrhage, inflammation and softening ensue; in short we get a sum of anatomical disturbances associated with most severe clinical symptoms. The *retia mirabilia* of the kidneys are likewise unfavourable to the free transit of the pigmentary particles; at least these organs stand next to the brain in the frequency with which they exhibit melanæmic pigmentation, in the form of black dots and striæ in their cortical substance, corresponding in position to the Malpighian bodies and their afferent vessels.

b. COAGULATION OF BLOOD IN THE VESSELS (THROMBOSIS).

§ 185. One of the most important chapters of general pathology is taken up with the causes and consequences of the coagulation of blood in the interior of the vessels. We shall content ourselves with so much of it as is needful to understand the histology of the process.

Coagulation is determined by two conditions; retardation of the blood-current, and irregularities on the inner wall of the vessel which increase the friction between it and the passing blood. Thrombosis often complicates many of those diseases of the vessels to which the ensuing section will be devoted. But coagulation from increased friction may indeed be often if not always referred to coagulation from stagnation; and that wherever the irregularities in question afford even the smallest recesses in which the blood may pause. We shall return to this subject when we speak of endocarditis.

§ 186. The proximate cause of coagulation is in every case a precipitation of fibrin from the blood. The fibrin is not contained in the blood as such; it is produced during the act of coagulation itself. *A. Schmidt* has established the interesting fact that the blood-corpuscles contain an albuminoid substance (globulin, fibrinoplastic matter) which forms an insoluble compound with a similar body (fibrinogen) contained in the liquor sanguinis, whenever the obstacles to coagulation are removed, or conditions favourable to coagulation are present. This insoluble compound is what we call "fibrin."

Recently precipitated fibrin is a colourless substance much swollen by imbibition. Two parts of fibrin in a thousand are enough to give the coagulum a jelly-like consistency. Recent fibrin is invisible under the microscope owing to its great homogeneity and transparency. These properties begin however to be modified from the moment that coagulation has occurred. The molecules of fibrin possess so high a degree of mutual attraction, that the mass continues to shrink, squeezing out more and more of the fluid contained in its meshes. A highly characteristic change in the microscopical appearances is associated with this separation of the solid and liquid constituents of the clot; in the homogeneous mass above alluded to, a number of little gaps and fissures make their appearance, between which the solidifying fibrin remains as a more or less delicate network composed of round threads.

§ 187. The above change may be observed wherever the field is not obscured by too great an abundance of corpuscular elements. But this is almost invariably the case when blood coagulates in the vessels. Red and white blood-corpuscles in vast numbers are entangled in the coagulated fibrin and mask the microscopic details of coagulation so completely, that we are unable to make out anything even in the finest sections through a hardened thrombus. We may consider it as settled that a precipitation of fibrin underlies thrombosis; that the subsequent contraction and the peculiar desiccation which the thrombus undergoes are certainly due to the above-described changes in the fibrin; but the microscope fails to demonstrate the presence of fibrin among the innumerable cells of the intravascular thrombus; and I may add that this fibrin never subsequently reappears.

§ 188. The recent thrombus is always of a dark red colour and a jelly-like consistency, like any other blood-clot. Its shape depends on that of the cavity in which coagulation has occurred. Cylindrical plugs are very common, occupying the entire *lumen* of a small vessel or one of medium size, and terminating in a conical point at the end turned towards the still pervious part of the channel (obstructing thrombi). Other clots do not block the vessel completely, but adhere to one side of its wall, exhibiting more of a ribbon-like aspect with a tongue-shaped end (lateral thrombi). Farther modifications are brought about by the secondary precipitation of fibrin which is everywhere caused by existing coagula when these are immersed in the blood-current.

Layer upon layer is deposited, and by this *continuous coagulation*, 1st, a lateral thrombus may easily be converted into an obstructing one; and 2nd, the coagulation may spread from one vessel to its neighbours. In the latter event, the intruding clot will at first be lateral, then obstructing, &c. The size and shape which the thrombus may ultimately assume cannot be determined *a priori*, and can only be predicted with some degree of certainty in a few cases, *e.g.* after ligature of arteries. With reference to these we have the following law to guide us: the coagulation never extends beyond the nearest pervious collateral branch, whether in a peripheral or a central direction. The peripheral coagulation is not as a rule of much moment; since, owing to the complete contraction of the arterial walls it usually forms a slender and barely perceptible thread.

§ 189. We may now proceed to consider the farther changes which occur in thrombi. A few preliminary remarks are indispensable however, about certain differences *in their primary structure.* Much depends on whether a thrombus has been formed rapidly, by some sudden accident, as *e.g.* when a vessel is tied and a certain quantity of blood, suddenly cut off from the current, coagulates forthwith; or whether it has been produced more gradually. In the former case the colourless and red corpuscles are so equally distributed throughout the clot, that on examining sections of it we find the colourless elements distributed at regular intervals throughout the mass of red ones. It is far otherwise where the coagulation begins and goes on gradually and slowly. As examples of this latter mode, we have the coagulation which begins in the superficial vessels of an amputated stump affected by diphtheritic inflammation, and which gradually spreads upwards into the veins; the thrombosis which occurs in the left auricle in cases of mitral contraction; thrombosis in varicose veins and aneurisms. In all these cases, with which we shall become more familiar when we study the diseases of the vessels, what is known as the "viscosity" of the colourless corpuscles comes into play, giving rise to a concentric lamination of the clot. The colourless corpuscles are glutinous, *i.e.* their protoplasm tends to adhere to solid bodies, to penetrate into their pores. Most of all does it incline to unite with the protoplasm of other leucocytes; so in the comparatively sluggish current of the veins we not unfrequently find the white blood-corpuscles joined in pairs; and it is only on account of the rapidity with which the blood is forced through the arteries, and repeatedly transmitted through a system of innumerable canals of very narrow calibre, that no permanent union between these elements normally occurs.

Assuming that a clot has reached a certain size, and that a fresh layer of coagulated blood has just been deposited upon its surface, it is clear that of all the blood-corpuscles which are carried past it, the colourless ones, owing to their glutinous properties, will be the first to adhere to it, and to become stationary in its outer parts; just as in *Recklinghausen's* experiments on suppurative inflammation, excited by the introduction of a finely-porous body into the subcutaneous tissue, the pus-corpuscles penetrate into the pores, and thickly infiltrate the margins of the foreign body. Well, a layer of leucocytes is deposited which clothes the thrombus for a time, until a fresh deposit of red coagulum takes place. In other words, the blood coagulates by fits and starts, and between each recurrence, a large number of leucocytes have time to attach themselves firmly to the surface of the clot.

On making a transverse section through a clot of this kind we see at once that it is permeated in every direction by a system of transparent lines which exhibit a more or less distinctly concentric arrangement. These lines correspond to the cross section of the layers of leucocytes which alternate with broader layers of ordinary red blood. We must accordingly distinguish between two kinds of thrombi, basing our division on the differences in their primary structure:

1. Non-laminated thrombi, originating in the sudden coagulation of an isolated quantum of blood.

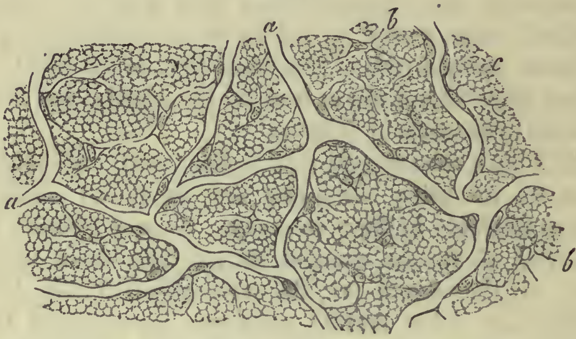
2. Laminated thrombi formed by an intermittent, gradual, and long-continued coagulation.

§ 190. A clot is susceptible of further metamorphosis in two different directions, that of organisation and that of softening. *Organisation*, or transformation into connective tissue, has hitherto been chiefly studied in the non-laminated thrombi of the larger vessels. The following account must therefore be understood to apply to these only, and must not be supposed to include the organisation of laminated clots, concerning which we are at present entirely ignorant. The thrombus attains its maximum size immediately after coagulation has taken place, when it still exhibits the dark-red colour and jelly-like consistency of a recent clot. It continues to contract from day to day till it shrinks up entirely, and after the lapse of a few months disappears, leaving not a trace of its former presence behind. This continuous decrease in size is associated with a decolorisation and condensation of its substance; it loses its original dark-red hue, until at length it comes to be only a shade redder than the wall of the vessel which contains it; it grows drier and more tough; whereas originally it lay loosely upon the walls of the vessel, at a later period it blends with them, assuming the character of a little plug of connective tissue, which seems rather to belong to the surrounding connective tissue and the wall of the vessel than to the blood. The progress of these alterations as seen by the unaided eye is elucidated by the microscope as follows:

§ 191. I have already said that in the recent non-laminated thrombus the colourless corpuscles are distributed among the red ones at tolerably uniform intervals. It used formerly to be supposed that all further changes started from these colourless elements. At the present day, the organisation of clots, in common with many other morbid processes, is explained by the activity of migratory corpuscles. Artificial thrombi have been produced by tying arteries in the lower animals; cinnabar has then been injected into the blood, and its leucocytes impregnated with this finely-granular material, which is easily recognisable under the microscope. It was found that those cells from which, on the second or third day after the occurrence of coagulation, the organising process appeared to set out, contained cinnabar; the inevitable inference being that they had migrated into the clot from without. These cells then put forth processes in various directions which meet one another and unite to form a delicate protoplasmic network with nuclei in its nodal points (fig. 71, *b*.) Even at this stage the structure of the clot might be compared to that of a connective substance; its corpuscular elements being represented by the leucocytes, and its intercellular substance by the mass of red blood-corpuscles and the fibrin. And this, if the phrase may be allowed, is the fundamental idea which underlies the whole organising process and which tends forthwith to realise itself.

Shortly after this primary differentiation has taken place, the vascularisation of the thrombus begins.* This conforms to the "tertiary" type, *i.e.* the opening up of capillary channels along the threads of the protoplasmic network. A more or less complete vascularisation may be demonstrated in every thrombus over eight days old, whether by injection, or by the examination of fine sections. The vessels are thin-walled capillaries with alternating nuclei (fig. 71, *a*); they get their blood mainly from the still pervious portion of the occluded vessel itself, whither also they return it, until other anastomoses are developed, though still in scanty number, with the *vasa vasorum*. An indispensable preliminary to the formation of such anastomoses is the perforation of the non-vascular *tunica intima* of the vessel, separated as it is from the middle coat by its homogeneous limitary membrane; and this is clearly a harder task for nature to perform than we might at first imagine it to be (fig. 72).

FIG. 71.



Transverse section through a clot produced by ligature of the crural artery, thirty-seven days after operation. Hardened in alcohol. Treated with dilute acetic acid and then with a little ammonia. *a*. Capillaries; *b*. The cell-network of the colourless blood-corpuscles. In the basis-substance we see the outlines of the red corpuscles.

§ 192. The vascularisation of the clot guarantees it a more durable and organic connexion with the body; it becomes henceforth a member of the series of vascular connective tissues. But how do matters stand with regard to the intercellular substance of this very peculiar connective tissue?

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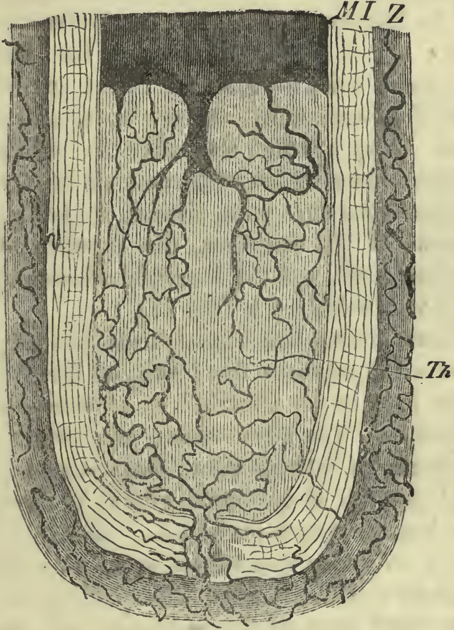
* See *O. Weber*, Handbuch der Allgemeinen und Speciellen Chirurgie, redig. von *Pitha* und *Billroth*. Bd. i., Lieferung 1, p. 143.

The red corpuscles together with the fibrin make up the bulk of the recent thrombus. Hence it is to alterations in *them*, that such changes in the clot as we are able to trace with the naked eye, must be chiefly due. The rapid escape of colouring matter from the red corpuscles explains the decolorisation of the clot; its shrinking and increased dryness are due to the contraction of the fibrin and the consequent expulsion of the contained fluid. What remains therefore is—1st, instead of every red corpuscle, a flake of colourless protoplasm; 2nd, the fibrin as an invisible but nevertheless very firm cement which binds these flakes together. The two form a mass which is not easily torn and which is never fibrous; from the first until about the

Fig. 72.



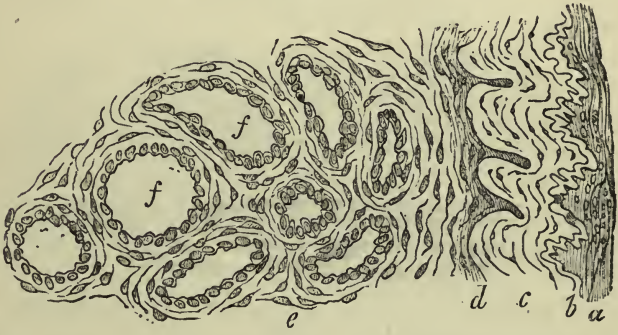
Longitudinal section through the ligatured end of the crural artery in a dog, fifty days after operation. Injected by *O. Weber*. *Th.* Thrombus. *M I.* Middle coat; *Z.* Areolar coat.

eighth week this constitutes the basis-substance of the thrombus. Moreover the original character of its constituent elements continues to be recognisable for a long time. In a thirty-seven days' old thrombus after ligature I found the decolorised blood-corpuscles so little altered in shape that their numbers entirely masked the vessels and connective-tissue corpuscles; and it was only after adding acetic acid, which made the whole specimen swell up violently and obliterated the outlines of the blood-discs, that the network of vessels and cells became distinctly visible. Then indeed its likeness to a vascular connective tissue became unmistakeable; and I do not scruple, on the ground of its reaction with acetic acid, to admit the direct conversion of the stroma of the blood-corpuscles into the basis-substance of connective tissue. I may add that even after the addition of acetic acid, a judicious neutralisation with ammonia rendered the outlines of the blood-discs once more distinct, so that both the constituent elements of the thrombus, the network of cells and vessels on the one hand, and the former blood-corpuscles on the other, could be seen side by side (fig. 71).

§ 193. The remaining histological alterations may be viewed as a cavernous metamorphosis (*see* § 129) of the thrombus. It used in former days to be described as a "sinus-like" (sinus-artig) degeneration. The blood-vessels grow wider and wider, while the parenchyma between them disappears and is replaced by a moderate quantity of colourless cicatricial tissue arranged in concentric laminæ round the vessels. At a certain stage in the process the cavernous structure is exquisitely apparent (fig. 73). The vessels continue to grow wider and the septa between them thinner, until they wholly disappear and the thrombus accordingly ceases to exist.

§ 194. The *softening* of thrombi contrasts with their organisation in much the same way as suppuration contrasts with organisation in the case of inflammatory products. This remark applies to the clinical significance, as well as the naked-eye peculiarities of the process. As regards the latter, a decolorisation of the primarily dark-red thrombus, plays here, as during its organisation, a prominent part. The colour begins to fade at its centre, and the decolorisation spreads from this point to the circumference; it is associated with a certain degree of condensation which is not however, as it is during organisation, a permanent, but a transitory phenomenon, and passes straightway into the opposite condition, that of softening and liquefaction; accordingly we find at a certain stage in the process a yellow fluid not unlike pus occupying the interior of the clot, and enclosed in a comparatively tough, flesh-coloured layer which adheres firmly to the wall of the vessel. The circumstance that softening occurs chiefly in laminated thrombi gives rise to various modifications in the anatomical appearances. The strata of colourless corpuscles sometimes exhibit a singular proneness to take part in the softening, while at others they offer the longest resistance to disintegration. In the former case, the connexion of the colourless cells with one another is early broken. Even before the red corpuscles have had time to part with all their colouring matter, the thrombus breaks up into a reddish-grey pulp which may resemble anything between chopped meat and the lees of wine.

FIG. 73.

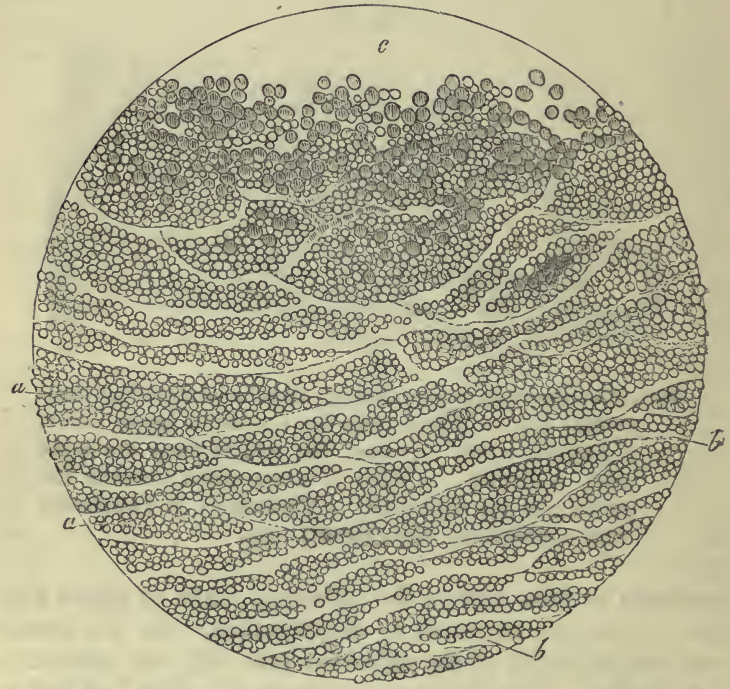


Part of a transverse section through an arterial thrombus three months old. *a.* Middle coat (its innermost layers only); *b.* Lamella which separates the middle from the inner coat; *c.* Intima; *d.* Line of demarcation between the intima and the thrombus; *e.* Thrombus; *f.* Vessels cut across; epithelium very distinct. $\frac{1}{300}$.

If on the other hand the white corpuscles offer a more determined resistance than the red ones, we first of all get a mass of cheesy colour and consistency, passing at a later period into a more spongy or loculose decomposition of the whole of the softening thrombus.

§ 195. I have also endeavoured to ascertain the histological details of the softening process. Fig. 74 represents a transverse section through a laminated coagulum, the centre of which has already undergone softening. The upper part of the drawing shows the boundary-line between the outer layers of the thrombus which are still solid, and its central portion which is already diffluent. The lower part shows the almost mathematical regularity with which the colourless dissepiments and the layers of red blood which they enclose alternate with one another. On a level with the softening edge of the clot the colourless striæ pass into rows of independent leucocytes, while the compact masses of red discs lose their cohesion and mingle with the fluid products of softening. They have already lost their colouring matter and

Fig. 74.



From a section through a softening thrombus. *a*. Layers of red blood-discs; *b*. Colourless layers consisting of white blood-corpuscles fused together; *c*. The cavity due to softening. $\frac{1}{300}$.

have become cloudy, so that they can hardly be distinguished from the white corpuscles proper; their stroma now becomes dissolved as well, giving the fluid products of softening a mucoid, often stringy consistency. The colourless cells also break up into minute granules. The resulting liquid contains therefore as a rule nothing but granular *débris* and oil-globules; and to these it owes its yellowish-grey puriform aspect; true pus-corpuscles (even if we include the colourless corpuscles of the blood under this name) occur only in very small number, and there is no question of any proliferation of corpuscular elements; so that to call the softening of thrombi a suppuration, though it does convey some idea of the naked-eye appearances, fails entirely to hit the essential nature of the process.

§ 196. The softening of thrombi is in more than one respect dangerous. First among possible mishaps, we have the chance that wherever the clot is freely exposed to the blood-current, bits of it may be detached and carried away. Should this come about, the fragments may be carried with the stream (*a*) from the radicles of the vena cava through the right heart into the lungs; (*b*) from the radicles of the pulmonary veins through the left heart into various organs of the body; (*c*) from the radicles of the portal vein into the liver. The distance to which they penetrate into the circulatory tract which they have entered depends upon their size. It is obvious that only particles no bigger than blood-corpuscles can travel without hindrance throughout the whole circulatory system. Any particle of larger size than this must be stopped somewhere or other, blocking the vessel in which it is arrested (Embolism).

Much might be said about the course emboli prefer to take. In the lungs they most frequently select those long, straight branches of the pulmonary artery which run along the inner surface of the middle and lower lobes to their edges and the neighbouring parts of their external surface. In the systemic circulation the larger emboli most frequently select the popliteal and Sylvian arteries. The embolus in these cases appears to follow the most direct route, that in which there are fewest turnings. It seems to happen not unfrequently that an embolus is driven against the projecting angle between two bifurcating divisions of an artery, and there broken up into smaller fragments like a floe of ice against the piles of an ice-guard. These fragments are distributed among the branches below the point of bifurcation. This affords an adequate explanation of multiple embolism in some one part of an organ while the rest is unaffected, as *e.g.* of a single Malpighian pyramid of the kidney, or a single lobule of the lung. Finally *O. Weber's* researches have established the fact that minute emboli may pass through the pulmonary capillaries to be ultimately arrested in the narrower capillaries of the kidneys.

§ 197. The consequences of embolism, the morbid changes which are produced in the organs whose vessels are plugged, will be more fully discussed in another part of the present work. I may say generally however that the primary and immediate consequence of every embolism is anæmia (ischæmia, arrest of blood supply), but that this bloodlessness is immediately followed as a rule by extreme congestion. The more complete the anastomotic connexion of the plugged vascular area with neighbouring regions, the better is it fitted to play the part of a cœcal appendage, a diverticulum of the circulatory apparatus, which is replenished with blood from every side, but which possesses no adequate outflow, so that the tension of the blood in its interior is higher than in all the other capillaries of the body. This secondary hyperæmia may lead to rupture of vessels, to hæmorrhagic infarctions; in any case the blood stagnates; it is not renewed and nutrition comes to a deadlock. The consequences of embolism therefore are all essentially bound up with disturbed nutrition; not a few indeed present the characters of true necrosis. (Cf. Metastatic abscesses of the lung, the liver, the kidneys, embolic necrosis of bones, yellow softening of the brain, &c.)

c. INFLAMMATION AND TUMOURS.

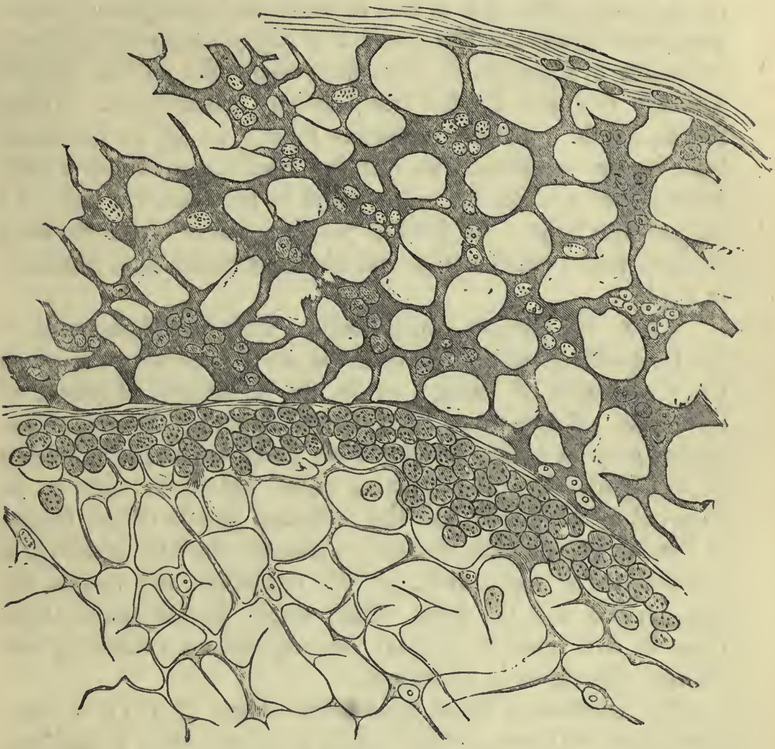
§ 198. The possibility of an inflammation of the blood (hæmitis—*Piorry*), was at one time seriously discussed. The increase in the number of leucocytes which may be shown to accompany leukhæmia, caused *Bennett* in particular to assume that the blood as a whole underwent suppuration. All such theories however must be rejected by us, were it only on the ground that the contrast between blood and parenchyma, between *nutriens* and *nutriendum*, is indispensable for our conception of inflammation. Hence we can only admit the existence of inflammatory—and we may add, of neoplastic processes generally—in those organs where the blood-corpuscles originate, viz. the lymphatic glands; on the other hand, we not only admit, but most distinctly affirm, that such inflammatory action may influence and alter the composition of the blood itself.

§ 199. A former attempt to define the leading characters of lymphadenoid tissue led us to the conclusion that it could not be better described than as a tissue in which an early phase of development—a phase very nearly allied to embryonic tissue—had become in a measure permanent. This circumstance must be borne in mind when we see how readily the lymphadenoid tissue may be induced to develope in any direction whatever, when prompted by an appropriate stimulus. Should the organs from which the lymphatic glands derive their lymph be inflamed, this may give rise to suppurative, caseous, and indurative lymphadenitis; the specific inflammations are all reproduced in the corresponding lymphatic glands; *e.g.* the syphilitic gumma, the miliary tubercle, the typhous product (§ 112); finally, almost all the carcinomata implicate the nearest lymphatic glands as a first step towards infecting the entire organism. Moreover, the morbid product, whatever it may be, manifests itself in the lymphadenoid tissue with a simplicity and completeness often lacking in the primary growth; to this rule there are but few exceptions; and hence it is that the lymphatic glands may be recommended as especially adapted for the investigation of the proper *structure* of a tumour. This however must not be taken to mean that the lymphatic glands are equally favourable for the study of the *development* of morbid growths; on the contrary, this is just the point at which our knowledge fails us most, as will be clearly enough seen from the following summary.

§ 200. I. *Acute lymphadenitis.* The internal condition of a lymphatic gland which, owing to inflammatory changes in the area of distribution of its afferent lymphatics, has become moderately swollen and tender, may be taken broadly to consist in hyperæmic distension of its vessels, together with an increase in the number of its contained lymph-corpuscles. Whence are these corpuscles derived? We may adopt one of three hypotheses to account for the fact, and bring very weighty analogies in support of each in turn. For instance, we may assume a migration of leucocytes to take place from the distended vessels; or a proliferation of the existing cells; or a transmigration of corpuscular elements from the seat of inflammation. It is unfortunate that we cannot decide which of the three views is the right one; for the settlement of this question would be most important for our knowledge of the physiological function of the lymphatic glands. On *a priori* grounds we are tempted to believe in an autochthonous proliferation of the lymph-corpuscles. We may very plausibly suppose that we have before us only a quantitative excess of the normal proliferative activity of the gland; of that process which satisfies the physiological requirements of the blood for young elements, and whose increased activity is perhaps intended to compensate for the disproportionate loss of colourless cells caused by their migration from the vessels in the inflamed region. But since erroneous preconceptions would in this matter be peculiarly hurtful, we must rigorously confine ourselves to the most temperate statement of observed facts.

According to *Billroth* (fig. 75) a section through the gland (after hardening), from which the cells have been thoroughly removed by pencilling (or better still, by shaking), shows a very marked overgrowth of that system of soft, protoplasmic, stellate corpuscles which is stretched out between the walls of the lymph-sinus. The cells swell up in due form, they anastomose more freely with one another, their processes grow thicker, and the nodal points more numerous. A luxuriant proliferation of the nuclei accompanies these changes, so that we finally get the appearance of multinuclear giant-cells, connected with one another by broad anastomoses. The reticulum in the interior of the lymphatic cords and nodules (Lymphstränge und Lymphkolben) remains at first quite passive in presence of the comparative abundance of the infiltrated cells. A large number of its finer threads are torn across, and the whole tissue comes to consist of only a limited number of main trabeculæ, which seem to be rather stouter than usual. It is only when the swelling takes place very gradually that all the trabeculæ of the reticulum undergo a reactive overgrowth; of this I shall say more anon. As the reticulum disappears the lymph-corpuscles form globular aggregates of larger size. Such aggregates exist here and there even in the normal lymphatic nodules; now however they permeate the whole of the glandular parenchyma. These globular masses of cells ought certainly to be regarded as centres of proliferation, although this does not admit of being directly proved. Whether the above-described transformation of the corpuscular elements of the retiform tissue of the lymph-path into giant-cells admits of a like interpretation, must remain doubtful; the earlier stages of cell-proliferation, namely fission of the nuclei and increase in the amount of protoplasm are indisputably present.

FIG. 75.



Part of a section through the cervical gland of a dog swollen to the size of a hazel-nut in consequence of inflammation of the lips, artificially excited. $\frac{1}{500}$. After *Billroth*. Showing the septum of connective tissue, the sinus terminalis and the marginal row of lymphatic nodules (Lymphkolben).

§ 201. Simple swelling of the lymphatic glands passes directly into suppuration of their parenchyma, provided always that the production and accumulation of lymph-corpuscles be not checked in time. Not only does the reticulum of the lymphatic nodules get worn progressively away, but the capillary vessels are ultimately torn across, and the corpuscular network of the lymph-path, rich as it is in nuclei and protoplasm, undergoes disintegration. The result is a richly corpusculated fluid, no longer distinguishable from pus, which fills all the cavities formerly occupied by the lymphadenoid parenchyma. When this occurs in a solitary lymphatic follicle, as *e.g.* in the intestinal mucous membrane, we call the resulting condition a follicular abscess; when an entire gland is involved, we term it a suppurating bubo. Its further progress comes under the head of suppurative inflammation and abscess-formation, as discussed in § 94.

§ 202. II. *Chronic lymphadenitis.* Chronic inflammation of the lymphatic glands differs from the acute form not so much in the slower rate of change, as in the permanent character of its results. Several very characteristic forms of chronic inflammation may be distinguished. First we have a true overgrowth of the lymphadenoid substance, which indeed is only to be observed in the tonsils and the follicular glands of the fauces. It consists in a uniform increase in amount of *all* the histological constituents of the follicle, *sc.* the reticulum, the vessels, the lymph-paths and the cells. Each single follicle attains from three to five times its normal volume, without exhibiting any striking alterations in its texture.

The leukhæmic form, considered above (§ 181), is most closely related (from an anatomical point of view), to this true overgrowth; it differs from it in bearing more of a functional character, and also in the mode of its causation; for it is not a result of repeated catarrh of the corresponding mucous surface.

§ 203. We come in the next place to a form of chronic enlargement which only occurs in individuals specially predisposed, and which is therefore regarded as pathognomonic of what is known as "Scrofulosis."

We employ the same word, in a more restricted sense, to denote the disease of the lymphatic apparatus; since our general conception of scrofulosis embraces the primary lesions together with the morbid state as a whole—the constitutional taint of the affected person. Those primary lesions are sometimes characterised by their destructive tendency, as in the lungs and the osseous system; sometimes too, they exhibit no special characters whatever. It is among the latter group that the glandular affection takes a prominent place, receiving the name of scrofulosis κατ' ἐξοχην.

§ 204. The tissue-changes which result in scrofulous enlargement of glands may be regarded in the light of a *partial* overgrowth of the gland-substance, in so far as they consist, not in a uniform increase in bulk of *all* its structural constituents, but in a multiplication and enlargement of *the cells only*, which make up the "enchyma" of the gland. I lay emphatic stress on the *enlargement* of the individual elements which accompanies their increase in number, because it appears to me that this enlargement is not only a constant phenomenon, but one which stands in an intimate relation to the numerical increase. For in the interior of the enlarged lymph-corpuscles a nuclear proliferation and endogenous cell-development take place, like that which we have already seen in the cells of tubercle, and that with which we shall hereafter become acquainted in the "typhous" deposit. It is interesting to trace the sequence of the morbid changes in the interior of a gland. We find that the first parts to become affected are those which are on the immediate brink of the stream of lymph, and which are consequently the first to be exposed to the pathological irritant brought from the peripheral seat of mischief. At a very early stage, the stellate corpuscles which traverse the lymph-sinus (across which they may be said to be stretched) begin to take part in the process by division of their nuclei and proliferation of new elements; this occurs partly at the circumference of the gland round the terminal nodules (Endkolben) partly in its medullary substance; in either case we have an infiltrated material of soft consistency, which appears of a dull-grey or reddish-grey hue to the naked eye, and which is present in largest amount, where, under normal conditions, a system of intercommunicating lacunæ separates the constituent parts of the gland from one another. As a result of this, the limits of contiguous lymphatic nodules (Lymphkolben) in the cortical substance, and of contiguous lymphatic trabeculæ in the medullary substance, are wholly obliterated; and in proportion as the proper substance of the lymphatic nodules and trabeculæ takes part in the pathological proliferation, the cut surface ceases to present any distinction of parts, and the whole gland appears converted into a homogeneous substance of a dull-grey hue.

This brings us to the culminating point of the whole process; the scrofulous bubo is about as big as a walnut when the unaltered gland was no bigger than a bean; according to the amount of moisture present, it may be either soft and flabby, or firm, elastic, and even springy. Meanwhile the process does not long remain stationary at this point. The newly-formed substance not only blocks the lymph-paths through the gland, but it also squeezes the blood-vessels to such an extent that the circulation is entirely arrested. It becomes impossible to force injection of any kind into those parts of the gland which are most swollen. With the arrest of the blood-supply nutrition of course ceases, and the gland falls a prey to "cheesy degeneration." Where this occurs, the grey mass loses its transparency; it then becomes yellowish-white, opaque, dry and friable. Should the entire gland have become cheesy, it resembles on section "a fresh potato—not indeed so moist, but quite as homogeneous, and of the same yellowish-white colour" (*Virchow*, Geschwülste, vol. ii. 593).

§ 205. The fate of the cheesy glands (Tyromata) appears to depend in the main upon their situation. For while in the mesenteric glands we nearly always observe a subsequent shrinking, due to the reabsorption of whatever fluid they may still contain, and sometimes also a deposition of earthy salts and consequent petrifaction, the lymphatic glands of the neck commonly end by undergoing softening. The cheesy deposit melts from centre to circumference into a yellowish whey, in which fatty-granular *débris* are suspended in flakes of variable size. When the whole of the cheesy matter has thus been liquefied, the parts immediately around the gland usually take on inflammatory action; and this prepares a way for the escape of the "scrofulous pus." When this has escaped, a "scrofulous ulcer" is left with its flabby, overhanging, bluish and congested edges. Finally the opening closes, and the point at which the abscess burst is only indicated by a puckered and stellate scar.

Virchow has recently described a third mode of retrograde metamorphosis which is certainly the most desirable one of the three. It consists in the complete resolution of the cheesy matter. It takes place, in all probability, by a liquefaction of the gland at its periphery, followed by absorption of the resulting fluid into the vessels of the capsule which are dilated by collateral hyperæmia.

§ 206. We have yet to speak of *chronic induration;* a phenomenon which belongs to the category of inflammation. Attention has already been called to the fact that it is only the *rapid* accumulation of lymph-corpuscles in the lymphadenoid substance which causes rupture of the reticulum; this of course implies the converse proposition, viz. that a *slow* and gradual increase in the number of the embedded cells is not followed by any such damage to the retiform tissue. Nay, we find the chronic changes associated with a very marked "reactive" thickening and elongation of all the trabeculæ of the reticulum. The latter accordingly increases in bulk to such an extent that the corpuscular elements come at length to occupy very little room in comparison, and the entire gland becomes tough and fibrous.

§ 207. III. *Syphilis.* The indurated chancre (§ 110)—the primary manifestation of constitutional syphilis—is followed by a chronic induration of the corresponding lymphatic glands; this is known as the "indolent bubo"; the induration however is due not so much to a hardening and quantitative increase of the reticulum, as to a very uniform though by no means luxuriant proliferation of young cells in all parts of the gland. Every vacant space is crammed with cells; and here the matter ends, at least for the time. Injection by simple puncture causes a similar, though of course only transient enlargement and hardening of the glands. This condition may remain unaltered for months and years together; it seldom proceeds either to a more acute inflammatory activity on the one hand, or to caseation and necrosis on the other. Ultimately, however, a fatty degeneration of the cells sets in, the *débris* are reabsorbed, and the gland returns to its normal state.

IV. *Typhous degeneration* (§ 112) of the lymphatic glands, as a specific result of corresponding lesions of the mucous membrane, will be discussed among the diseases of mucous membranes. The histology of the process is characterised by a cell-form which has already been briefly described in § 112.

§ 208. V. *Sarcoma.* Lymphadenoid sarcoma has its prototype in the tissue of the lymphatic glands; hence these are among its most favourite localities. It begins as a simply hyperplastic enlargement; at a later period it assumes its true character as a progressive growth. Several subspecies may be based on its variations in consistency and colour, in rapidity of growth and malignity. The least malignant forms, whose growth is least rapid, and whose texture is hardest, are characterised by the simultaneous implication of a whole group of glands, *e.g.* of all the glands of the upper or lower cervical fossa. A highly lobulated tumour is produced, often of large size, every one of whose lobes corresponds to a swollen lymphatic gland. The vessels and nerves are variously dislocated, and the removal of the mass by operation rendered almost impracticable in consequence (Pseudoscrofulosis).

A second variety, much softer than the first, and made up of larger cells, is especially prone to perforate the walls of veins and then to extend in their interior (cancer of veins). We sometimes find all the veins in the front of the neck or in the groin filled with sarcomatous thrombi of this sort; these of course afford excellent materials for embolic accidents. The precise mode in which this intravascular extension takes place has not yet been satisfactorily ascertained. From microscopic investigation one gets the idea that the first step is a coagulation of the blood, and that the farther growth of the sarcomatous mass proceeds as it were under cover of this clot. Others again assert that the clot is directly converted into sarcomatous tissue.

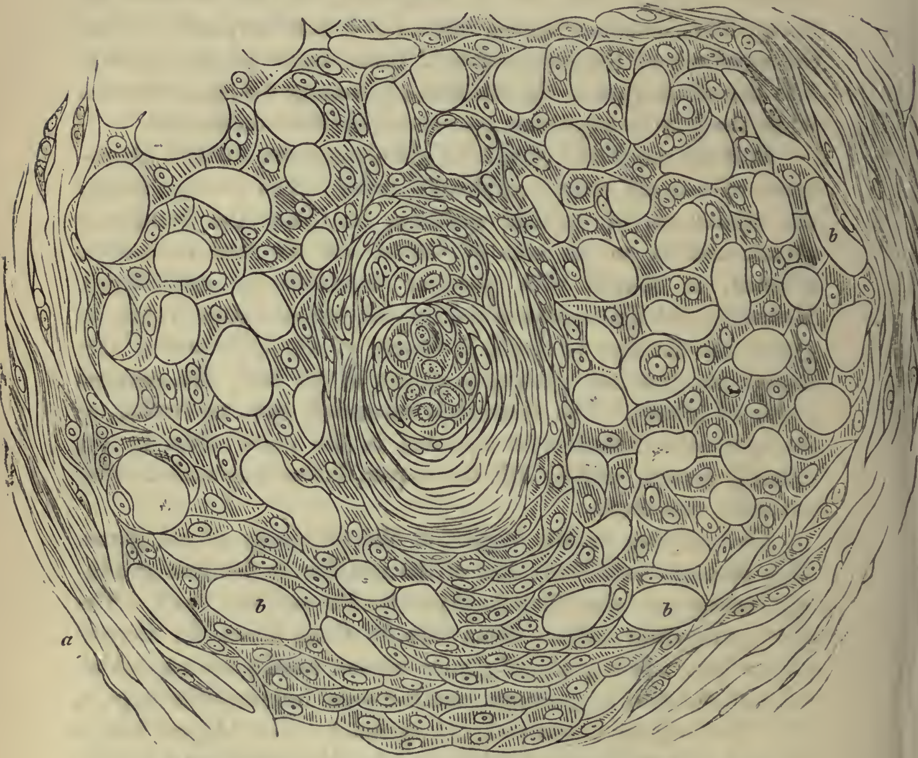
A third set of lymphadenoid sarcomata are marked by their tendency to break through the limits of their parent-gland at an early period, and to cause extensive infiltrations of the loose areolar tissue in its neighbourhood. In rapidity of growth and malignity, these tumours do not yield the palm to any species of sarcoma, though they never exhibit an alveolar structure. As regards treatment, they ought not as a rule to be meddled with, although the observations on the fatty degeneration and absorption of sarcomata in consequence of intercurrent erysipelas, given in § 92, referred to this very species.

§ 209. VI. *Carcinoma.* One of the most interesting problems in histology is the discovery of the way in which a primary cancer infects a neighbouring lymphatic gland; and should the *a priori* hypothesis, that it is due to a migration of cancer-cells from the primary growth, turn out to be well-founded, it is desirable to ascertain farther, the exact point at which these cells are arrested, and how they give rise to the first nests of cancer-cells, whether by proliferation or by infecting the adjacent lymph-corpuscles. After many investigations specially directed to this point, I can only say that the transformation of the lymphadenoid tissue into the substance of a glandular cancer takes place very simply; the trabeculæ of the reticulum increase markedly in length and thickness (just as in chronic induration), its meshes become enlarged from ten- to twenty-fold, and are occupied by the specific elements of cancer instead of lymph-corpuscles. Thus the structure of the lymphadenoid tissue seems to pass directly into that of the cancer, the reticulum becoming the cancer-stroma while the lymph-corpuscles are converted into cancer-cells.

Epithelioma of the lymphatic glands presents us with phenomena of a much more complicated order. The law regulating the metastasis of morbid growths, *sc.* that the lymphatic glands nearest to the seat of disease are the first to become affected, is obeyed with peculiar strictness by epithelioma. Hence in epithelial cancer of the lips, the submaxillary lymphatic glands are the first to swell, in cancer of the penis or the labia majora the inguinal glands, in cancer of the scalp the cervical group of glands. The metastasis commonly goes no farther, as the extensive disturbances operated in the mean while by the primary growth usually kill the patient before any such further extension can occur.

The swelling usually begins at the periphery of the gland. This becomes nodulated; one of the nodular projections gradually increases in size till it incorporates the rest into itself. The gland ultimately attains from two to three times its normal dimensions. In a group of glands we can usually see one which exhibits the first beginnings, another some intermediate stage, a third the highest degree of enlargement. The biggest lumps (equal to a pigeon's egg in size), nearly always contain a central cyst due to softening. The smaller and smallest ones are distinguished by their white colour and their tough, dry consistency, which contrasts sharply with that of the unaltered portions of the glandular parenchyma. This normal parenchyma however, at least in the neighbourhood of the smallest nodules, is normal only in seeming. The microscope proves that it has already undergone some very interesting changes, which enable us to judge of the mode in which the mass of epithelial cells first originates. If we follow up the well-known epithelial cylinders to their origin, we shall find the earliest signs of the approaching change to consist in the aggregation of from two to five epithelial cells in spaces of unusual size, which are not bounded by the delicate lymphadenoid reticulum, but are meshes in that network of nucleated, protoplasmic corpuscles which traverses the peripheral lymph-sinus and the lymphatic channels of the medullary substance. I believe these epithelial cells to have migrated from the primary growth, and I regard the character-

Fig. 76.



Epithelial cancer. Origin of the smallest nodules in the retiform tissue of the lymph-path of the gland. *b*. Meshes of the reticulum; *a*. Adjoining connective tissue.

istic changes which the cells of the reticulum in their neighbourhood have undergone, as a result of "epithelial infection"; for they increase in size, and their anastomoses become broader, the final result of these changes being a structure (fig. 76) which recals in some degree that of the secreting network of the liver. The frequent occurrence of double nuclei points to an independent multiplication of the cells by fission. In the face of this appearance, and of the fact that the alteration is only met with in the neighbourhood of mature, concentrically laminated epithelial cells, can we hesitate to believe that the cells of the reticulum are actually converted into epithelial cells? I ought to add, that the retiform structure persists for a long time, and may even be demonstrated in cancroid nodules which are large enough to be recognised by the naked eye.

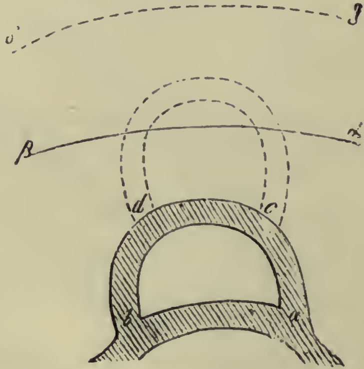
II.—MORBID ANATOMY OF THE CIRCULATORY APPARATUS.

1. Diseases of Arteries and Veins.

§ 210. Before entering on the pathological histology of the vascular system, I must say a few words about its normal structure; and this chiefly because current expositions of the subject leave several disputed topics undecided; inasmuch however as these are most important for the due appreciation of morbid changes, I feel bound to express my opinion concerning them at the outset.

As might have been anticipated *a priori*, all the vessels of the body are constructed on a uniform plan—which is best elucidated by tracing the course of their development.

Fig. 77.



Let *a*—*b* represent a capillary loop, and α—β the boundary-line of a growing organ. The blood flows from *a* to *b* under a certain pressure, at a certain velocity, and with a certain tension of the vascular walls. Let the pressure, the velocity and the tension be each represented by unity. Now when the progressive growth of the organ transfers its boundary-line from α—β to γ—δ, the capillary loop *a*—*b* will no longer suffice to carry on the nutrition of the extended vascular territory. A new capillary loop, *c*—*d*, is produced. Like every vessel in the organism, this springs from a pre-existing vessel. Suppose, what is quite possible, that its two extremities are implanted into the capillary loop *a*—*b*, in just the same way as the loop *a*—*b* is connected with its parent-vessel. The enlargement of the blood-path entails an increase in the amount of blood, so that the current passes through *c*—*d* under the same pressure, velocity and tension as it did through *a*—*b*. But these values do not continue the same for *a*—*b*. Taking a transverse section through *a*, we see at once that through it flows not only the blood which fills the capillary loop *a*—*b* under a pressure, velocity and tension each of which equals unity, but also the blood which goes to fill the loop *c*—*d*. Assuming that *c*—*d* equals *a*—*b* both in length and sectional area, the pressure, velocity and tension at *a* must each equal two. Continuing this train of reasoning, and assuming that with the farther growth of the organ, fresh capillary vessels are again and again projected from the old ones, the pressure, velocity and tension must increase proportionately in the afferent and efferent vessels; greater demands will be made on the resisting power of the transverse sections *a* and *b*. We might accordingly expect to find the vessel increasing in calibre and its walls growing progressively thinner. It does in fact increase in calibre, but its wall does not grow thinner; a peculiar law, which regulates the growth of the entire vascular system, comes into operation at this point, a law according to which any increased demand upon the resisting power of the transverse section of a vessel, is met by a proportionate thickening of its walls (hypertrophy and dilatation). The wall of the vessel grows thicker, one limb of the capillary loop becoming an afferent artery, the other an efferent vein.*

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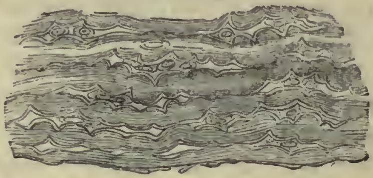
* Strictly speaking, our scheme is only applicable to cases in which a capillary area is provided with a single afferent and efferent vessel, *i.e.* to *retia mirabilia*. In order to make it suit *all* the varieties of circulatory distribution throughout the body, it is necessary to add that anastomoses between neighbouring capillary areas render the formation of larger and finally of absolutely large vascular territories possible, the artery of one area bringing enough blood for both, while one vein

§ 211. No one has ever yet seen the actual details of the process by which a capillary vessel is converted into a small artery or vein. In this as in many other cases, we are compelled to draw our conclusions as to what actually occurs, by inference from what has gone before or what comes after. The wall of a capillary vessel consists of a homogeneous, glassy membrane beset at intervals with nuclei. By impregnating this membrane with silver nitrate we are able to prove that it is made up of plates accurately adapted to each other; to about the middle of each plate a nucleus is fixed by a little soft protoplasm. The plate itself may be viewed as a thin layer of hardened protoplasm. The capillary membrane passes uninterruptedly into a somewhat thicker, vitreous lamella which exists in all the arteries and veins, even in the aorta, at the junction of the internal with the middle coat; this lamella may always be recognised in transverse sections, not only by its greater lustre, but by the uniform sinuosities of its double contour, which are due to the fact that owing to its deficient elasticity, it follows the variations in calibre of the vessel, not by alternate condensation and rarefaction, but by becoming folded and unfolded (fig. 73, *b*). On the inner surface of this membrane, the tunica intima and epithelial lining are developed; on its outer surface the muscular coat and tunica adventitia. The necessary materials are furnished by proliferation of the cells of the capillary wall, as may readily be seen in the arterioles (Uebergangsgefässe).

FIG. 78.



Vertical section through the inner coat of the aorta. For explanation *see* text. $\frac{1}{500}$.

The tunica intima of the larger arteries and veins exhibits the same appearances both in longitudinal and transverse sections;

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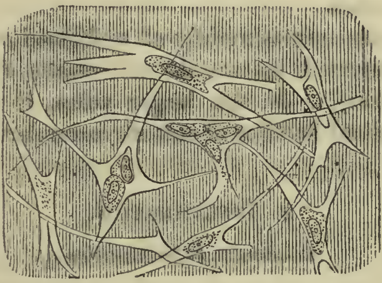
suffices to return the blood from both areas to the heart. It is obvious that such modifications cannot alter the main gist of the observations made above.

I refer to the striated lamellæ of *Henle*, which present themselves under a magnifying power of 500 diameters (fig. 78) as finely striated, wavy layers of basis-substance (of connective tissue), in whose interstices flattened, lenticular corpuscles are embedded. In these cell-containing spaces, the opposed surfaces of the basis-substance exhibit a peculiar, homogeneous lustre; moreover, they present a double contour, which makes each cell appear as if surrounded by a special capsule. The plausibility of this view is enhanced by the appearances presented in horizontal sections (fig. 79) which show how closely this peculiar property of the basis-substance is connected with the distribution of the cells. The cell-containing spaces appear of a stellate form, with branching prolongations which anastomose with one another. The whole arrangement reminds us very forcibly of the cell-containing capsules of cartilage. But can we be sure that the stellate capsules of the intima are really closed cavities? For it is undoubtedly true that in those morbid products which spring from the intima, the newly-developed cells are found outside the "connective-tissue corpuscles," as well as within them; this forces us upon the horns of a dilemma; for either they cannot have sprung from these connective-tissue corpuscles, or else they must have escaped from the capsules. We may provisionally regard them as leucocytes which have migrated from the blood.

FIG. 79.



Horizontal section through the inner coat of the aorta. For explanation *see* text. $\frac{1}{500}$.

The structure of the intima has not hitherto received the attention which it merits; on this ground, and also with a view to its diseases, which we are about to consider, I have lingered rather long over it. I may be all the more brief in my remarks concerning the two outer coats. The media, composed of smooth muscular fibres, constitutes the main bulk of all the larger vessels. The transverse, nucleated spindle-cells impart a highly characteristic, annulose appearance to the smallest arteries and veins; in the larger vessels the muscular fibres are disposed in bundles in a framework of fenestrated lamellæ of elastic tissue. From three to ten or more principal lamellæ, separated by regular intervals, lie parallel to the surface of the vessel; each lamella being connected with its neighbours on either side by oblique buttresses. These buttresses are also fenestrated, so that the muscular bundles can pass uninterruptedly from one compartment to another.

The adventitia consists mainly of unformed connective tissue abundantly permeated by vessels and elastic elements (membranes and fibres). In the larger veins, it may sometimes contain longitudinal bundles of smooth muscular fibre.

a. INFLAMMATION.

α. *Acute Inflammation.*

§ 212. The phenomena of acute inflammation of the vessels are intimately connected with those of coagulation in their interior; for they are exclusively, or almost exclusively confined to parts where a softening blood-clot is in immediate contact with the inner wall of a vein or an artery, irritating the coats of the vessel by the diffusible products of its disintegration. This coincidence is so frequent, that it formerly led *Dupuytren* to invert the real order of sequence—to regard the acute inflammation of the vascular wall as the antecedent, and the coagulation of the blood as the consequent.

Even the most weighty and thorough changes operated by acute inflammation are by no means striking to the naked eye. We notice a hyperæmic state of the vasa vasorum, particularly at the junction of the media with the adventitia, and a thickening of the vascular coats to three or four times their normal diameter, so that an inflamed vein may not be distinguishable on transverse section from an ordinary artery. The normal smoothness of the inner surface gives place to a cloudy, opaque, or even velvety aspect. In rare cases, we notice little collections of matter, forming pustular elevations of the intima. The microscope tells us much more about the condition of a vessel thus altered. Its entire wall is in a state of inflammatory proliferation. Thousands of young elements, which may be summarily termed pus-corpuscles, lie between the fibres of the adventitia, between all the layers of the muscular coat, between the striated lamellæ of the intima. In the adventitia, besides the cells, I have occasionally found larger aggregations of an amorphous, jelly-like material, which I regard as coagulated lymph; here also, as well as in the outer layers of the muscular coat, extravasations occur, which extend along the vessel for a variable distance. It seldom happens that the pus-formation in the external coat goes so far as to cause abscesses. When it does, the abscesses are like long streaks of creamy pus following the course of the vessel; they must not be confounded with vessels which may happen to be filled with softened thrombi. The intima is less constantly involved in the morbid process; indeed I might almost say that in the majority of cases the intima is less altered than either of the other coats. It depends for its nutrition so much upon the blood which circulates in the vessel, that the occurrence of coagulation at once cuts off its chief source of pabulum, and leaves it a prey to necrosis, unless, as in the organisation of thrombi, vessels are forthwith developed in the coagulum. The passive behaviour of the intima must therefore be attributed to its lack of vital energy and nutrient material; and this view is confirmed by the observation that the farther progress of the mischief not unfrequently results in a true necrosis of the intima and its detachment from the middle coat.

§ 213. Apart from thrombotic arteritis and phlebitis there is hardly such a thing as acute inflammation of the walls of vessels. On the other hand, I must remind the reader that the vessels are continuous by their adventitia with the general connective tissue of the organs—that, rightly understood, the walls of the vessels are really a part of that connective tissue, and are therefore capable of taking a most active share in all inflammations, however acute, of the various organs in which they ramify. Indeed we shall find that in many of the inflammatory disorders of internal organs, *e.g.* of the pia mater, kidneys, &c., the chief seat of the morbid changes is in the adventitia and the immediate neighbourhood of the vessels.

β. *Chronic Inflammation.*

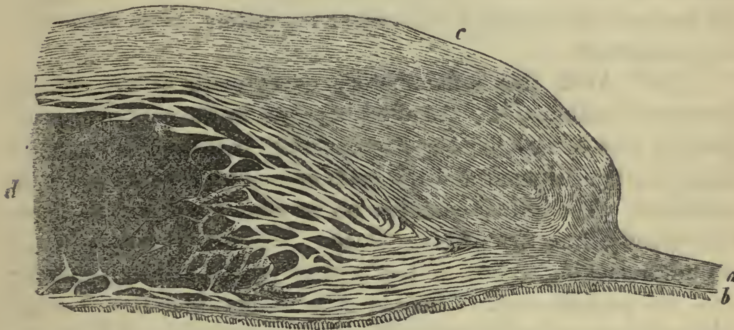
§ 214. Chronic inflammatory changes may occur in every part of the vascular system; but they are nowhere so important as in the internal coat of the arteries, where they give rise to the *endoarteritis chronica deformans* of *Virchow*. The view that this disorder (also known as atheroma) is of an inflammatory character, is by no means of recent date. A peculiarly transparent material which projects above the level of the intima, and which, as will presently be seen, is nothing more than the altered intima itself, used to be regarded as an inflammatory exudation, and the entire process was accordingly viewed as an exudative inflammation. An obvious objection to this view is that the exudation, in its quality of liquor sanguinis, had no occasion to coagulate at the very moment when it was reunited with its parent fluid. Accordingly, *Rokitanski* started the theory that the substance in question, though really coagulated fibrin, had not exuded from the vasa vasorum, but had been precipitated at the inflamed point of the vascular wall (where it formed a deposit), from the blood-current itself. This position likewise came ultimately to be untenable. *Lobstein*, and after him *Virchow*, taught us to look for the essential part of the process in an alteration of the proper tissue of the intima, and to eliminate whatever substances might afterwards have been deposited at the seat of mischief from the blood. *Virchow* laid the foundations of our present theory concerning the morbid change in question.

§ 215. It consists in a chronic inflammation of the inner coat of the vessel. True, we cannot detect all the cardinal symptoms of inflammation, but only swelling and perhaps impairment of function; but the finer alterations which the intima undergoes are throughout analogous to those which occur in connective tissue under the influence of prolonged irritation. There are many grounds for thinking that a mechanical irritation of the vascular wall may be at least *one* of the causes to which the morbid changes are due. For these are chiefly found at such points as are exposed to the full stress and impact of the blood; *e.g.* the upper curvature of the aortic arch, the points of origin and bifurcation of the vessels. Still, mechanical irritation must not be regarded as the sole cause of the disorder, though it determines its localisation. Among other predisposing causes are advanced age and free living, especially a free use of alcoholic stimulants. The etiology of gout is very similar to that of endoarteritis; hence the two diseases are often found together.

§ 216. The common starting-point of all the lesions due to chronic endoarteritis is to be found in certain flat and smooth, seldom tuberous elevations on the inner coat of the arteries. They rarely project more than a line above the surface; their margins are very irregular. At the point where a vessel is given off, they encircle it ring-fashion. They vary to some extent in colour and consistency, yet they may be generally described as bluish or reddish grey and cartilaginous; sometimes they may exhibit more of a gelatinous or mucoid consistency.

As regards the microscopic appearances, let me insist once more on the fact, of which we may readily assure ourselves by examining sections through the margins of the swollen part, that the outermost lamella of the intima, which is usually least altered, passes uninterruptedly over the surface of the swelling; that the change consists therefore not in a deposit *upon*, but in an actual thickening *of* the membrane itself (fig. 80, *a*—*c*). We may further regard it as certain that we have to do with a proliferation *in* and *from* the connective tissue of the intima, which has caused a positive increase in its bulk; young cells in countless

FIG. 80.



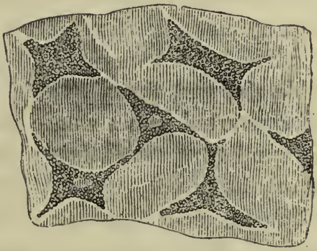
Chronic endoarteritis. Section through an indurated elevation of the inner coat, which is already undergoing fatty degeneration in its interior. $\frac{1}{25}$; *b*. Junction of inner and middle coats; *a*. Inner coat; At *c* this is hyperplastic and thickened, while at *d* it has become converted into an atheromatous abscess. For details *see* text.

numbers are everywhere distributed between the lamellæ; here and there we come upon larger aggregations of such cells. From these nest-like deposits, as centres, new systems of concentric lamellæ of connective tissue originate, which are intercalated between those already existing, thereby dissociating them from one another. For the production of fibrous intercellular substance advances *pari passu* with the multiplication of corpuscular elements; the latter never preponderate to such an extent as to make the products in any way resemble pus. We rather meet with scattered patches in which a soft, mucoid character of the intercellular substance is associated with a retiform arrangement of the cells—patches, therefore, of mucous tissue. Taking the phenomena in their entirety however, we cannot but be struck with the close similarity of the morbid products to the normal texture of the intima; hence we must regard the first stage of the process, the so-called sclerosis of the intima, as an *inflammatory overgrowth.*

§ 217. With this inflammatory overgrowth of the intima, the process culminates. As often happens in the case of morbid growth, time brings about a disproportion between the means of supplying nourishment and the mass of material which has to be nourished. The intima contains no vessels. It draws its pabulum directly from the passing blood. The vasa vasorum, which are never lacking in any of the greater vessels, barely penetrate into the middle coat. Should the intima therefore become thicker, those of its layers which are farthest removed from the nutrient fluid, *i.e.* the outermost layers, those next to the middle coat—will be the first to suffer from lack of nourishment. And here, two modes of retrograde tissue-metamorphosis may be observed side by side. The first and most extensive of these is a *fatty degeneration* of the cells, combined with solution of the intercellular substance. The naked eye detects in the interior of the hardened elevation, just upon the limits of the media, opaque yellowish-white striæ, running in a direction parallel to that of the surface, and uniting to form a more equably yellow spot. Should the morbid change be more advanced, this is replaced by a "focus of softening" of variable size, occupied by a friable or greasy pulp of the same yellowish hue. The presence of cholesterin crystals in large numbers gives this "atheromatous pulp" a spangled lustre. Should the focus of softening have attained larger dimensions by the progressive liquefaction of the indurated tissue, should it *e.g.* be separated from the blood-current by only a thin layer of unaltered intima, we call it an *atheromatous abscess.* When this layer at last gives way at its thinnest part, the pulp mingles with the circulating fluid, the base of the "focus of softening" is laid bare and we have an *atheromatous ulcer.* (For continuation *see* next section.)

Figs. 80 and 81 are meant to elucidate the histological details of atheromatous change. In fig. 81 we see, under a high power, that the fatty metamorphosis of the cells of the intima presents itself as a distension of the stellate interstices of its connective tissue with oil-globules. It would seem however, as though these preformed lacunæ were the depositaries of *all* the fatty *débris*, including those derived from the younger and more scattered cells, since a vertical section through an atheromatous abscess (fig. 80) shows the oily *débris* to be infiltrated into fusiform spaces, separating the contiguous lamellæ of the intima from one another. These fusiform cavities undoubtedly correspond in position to those points at which the cells are intercalated between the lamellæ of the intima (fig. 79). The greater the amount of oily *débris*, the longer and the thicker (in transverse sections) grow the spindle-shaped cavities; the lamellæ are forced farther and farther apart, and are finally softened and disintegrated; whereupon the oily matters forthwith unite to form a greasy pulp which fills the cavity due to softening (Erweichungshöhle). (Fig. 80, *d.*)

FIG. 81.



Connective-tissue corpuscles of the intima in a state of fatty degeneration. $\frac{1}{500}$.

§ 218. The form and size of atheromatous ulcers naturally vary quite as much as those of the indurated swellings which preceded them. They are at first sinuous; *i.e.* a probe passes through a small hole into a cavity which burrows some way underneath the surface. This cavity is that of the former abscess; it may be more or less distended with coagulated blood; as a rule it is empty. Moreover the thin membrane by which it is still roofed in, has a tendency to roll up from the hole to the margins of the cavity—the aperture increasing proportionately in size; more rarely, it is detached in shreds; in any event, the open atheromatous ulcer forms so marked an inequality of the surface, that it may readily give rise to coagulation; the adherent thrombi may be of considerable length, hanging from the wall of the vessel into its interior.*

§ 219. The second mode of retrograde metamorphosis which is met with in association with atheromatous degeneration, also begins as a rule in the deeper parts of the indurated intima. It consists essentially in an impregnation of the intercellular substance with earthy salts—a *calcification.* It gives rise to bone-like plates of variable size and form, often so large that *e.g.* the entire aortic arch is converted into a single bony tube. We not unfrequently find a number of small bony lamellæ, not exceeding half-an-inch in any diameter, scattered through the intima; the finger at once detects their presence. When shelled out of their capsules, most of them exhibit a saucer-like depression which corresponds to the curvature of the vessel; their edges are sharp. These edges are the first to perforate the superjacent layers of the intima, forming jagged projections and affording fresh opportunities for the production of thrombi. The partial detachment of larger bony lamellæ in consequence of fatty degeneration of the surrounding parenchyma is not unusual; complete separation however is rare.

I have never been able to convince myself that true bone is really formed, although this might fairly be inferred from the process being usually designated "ossification." The lamellæ of the intima are simply calcified and may be restored to their previous state by treatment with dilute hydrochloric acid; its cells however have ceased to exist; I have never seen anything worthy of being called a bone-corpuscle.

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* In the interior of an atheromatous deposit which was nearly quite softened, I observed a small, button-like, soft mass, which contained blood-vessels and had evidently grown from the middle coat. On more careful examination I discovered a whole series of such buttons under the same indurated patch. They consisted, apart from the capillary loops, of hyaline mucous tissue whose cells had undergone fatty degeneration. (20th July, 1867.)

§ 220. So much for chronic endoarteritis in the narrower sense of the term. An adequate estimate of the extensive lesions which it causes, especially in the aorta—lesions which, in advanced cases, may leave hardly a square inch of its surface intact—can only be formed from personal observation. To render our anatomical sketch of the disease complete, we ought to say something about two other processes, which the practitioner is not at the pains to distinguish very strictly from chronic endoarteritis, inasmuch as they are in fact very commonly combined with it.

First then, a fatty degeneration of the intima may exist, without any previous inflammatory overgrowth of the membranes—a morbid change which is simply degenerative from the first, and of whose immediate causes we know nothing. Histologically, the process is exactly like atheromatous degeneration; a fatty transformation of the cells (fig. 81) being followed by a gradual liquefaction of the lamellæ. This "fatty erosion" (fettige Usur) of *Virchow*, starts immediately from the inner surface of the vessel, and progresses from within outwards, destroying the intima layer by layer. Moreover, the disease is always confined to small, sharply circumscribed spots; in the aorta and larger arteries it causes a very pretty marbling of the surface, the affected parts being rough, opaque and velvety.

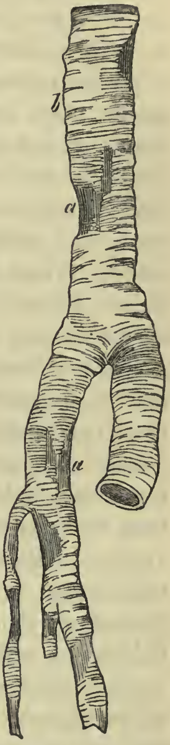
"Fatty erosion" is often met with in persons otherwise quite healthy. It must, however, tend directly to impair the resisting power of the vessels. Experience tells us that when once the intima is wholly destroyed, be the perforation ever so small, the muscular media, notwithstanding its thickness, is unable to cope with the pressure of the blood. The muscular fibres are separated from one another, and a transverse fissure results, through which the blood forces its way, either producing a *dissecting aneurism* by peeling off the adventitia, or else bursting through it and escaping externally. This explains the frequency of hæmorrhages into the most diverse organs, occurring in connexion with atheroma (*e.g.* the brain, kidneys, &c.). Moreover, fatty erosion of the inner coat has a certain share in causing the transverse rupture of the aorta which leads to dissecting aneurism of that vessel. This accident is usually regarded as simply a result of the concomitant hypertrophy of the left ventricle. The rent is usually situated about a finger's-breadth above the semilunar valves; it extends at first only through the internal and middle coats; the adventitia is peeled from the media; the blood tunnels its way between them, upwards as far as the heart, downwards as far as the descending aorta; it never gets as far as the abdominal aorta. When the sac thus formed is stretched to the utmost, a second rupture occurs, either outwards into the mediastinum, or (a rare event) inwards into the aorta at another point, so that for a short distance, the blood travels along two parallel canals. On examining the edges of the ruptured intima we occasionally find them in a perfect state of fatty degeneration; further investigations however are required, before we can decide upon the frequency and causal moment of this complication.

§ 221. Another, and a tolerably constant complication of chronic endoarteritis is *calcification of the middle coat.* This is not so prevalent in those parts of the arterial system which are chiefly predisposed to endoarteritis (such as the aorta and its main divisions), as it is in the relatively thick muscular coat of the smaller and smallest arteries, in those of the arm and leg, in the temporal arteries with their branches. Here too the process is one of simple petrifaction; calcareous salts are deposited in the muscular fibre-cells, which reappear unaltered when the salts are removed by acid. Even without the aid of the microscope the probable seat of the calcification may be determined; since the distinctly annulose aspect of the infiltrated parts can only be attributed to the transverse arrangement of the muscular fibres (fig. 82).

Calcification of the middle coat, as an independent affection, apart from atheromatous change, is more rare. In cases of calcareous metastasis (cf. § 51) all three coats of the vessel are uniformly infiltrated as a rule.

§ 222. Let us now inquire what influence the above-described alterations in the walls of the vessels may exert upon the movement of the blood through them. These alterations may be summarily classed under two heads: 1st, narrowing of the calibre of the vessel; 2nd, rigidity of its tube. This rigidity, mainly due to calcification of the intima as well as of the media, causes a certain proportion of the *vis a tergo* of the heart to be in some measure fruitlessly expended in the production of heat, and thus wasted so far as the propulsion of blood is concerned; whereas it would, under ordinary circumstances, have been stored up in a potential form, as tension of the elastic walls of the vessels, ready to be reconverted at any moment into active energy. Rigidity of a vessel therefore, while consuming the propelling force of the heart, indirectly diminishes the velocity of the blood-current beyond the rigid point. Contraction of the tube from swelling of its walls produces the same sort of effect, and that directly, by opposing inclined planes to the current of the blood; a variable proportion of the velocity is thus (according to well-known mechanical laws) partly converted into pressure, partly wasted as impact. Beyond the rigid and contracted part of the vessel therefore, the movement of the blood is slower than it should be. This retardation of the current manifests itself especially in the extreme parts of the systemic circulation, in the toes, finger-tips, and nose. It may even amount in these parts to complete stagnation, and so lead to what is known as "spontaneous gangrene" (cf. § 9) an accident to which old people are liable. The state of things on the proximal side of the rigid and contracted part is the opposite of that just described. We know that the pressure of the blood at any point of the vascular system is proportionate to the resistance to be overcome. If the resistance is augmented (as it is both by rigidity and by contraction) the pressure increases proportionately in those parts of the vascular system which are behind the obstruction. Increase of pressure in the entire aortic system is therefore a common result of atheromatous changes. This stands in a complementary relation to the diminution of pressure and velocity beyond the contracted and rigid parts. It is self-evident however that such increased pressure cannot last long without giving rise to farther consequences. Among these may be noticed:

Fig. 82.



Arteria cruralis with its branches. Middle coat calcified. Natural size.

1st, hypertrophy of the left ventricle; 2nd, dilatation of the affected vessels. Each of these changes tends to compensate for the primary lesion; hence it is that the hypertrophy is inversely proportionate to the dilatation.

b. Dilatation of the Vessels.

α. *Dilatation of Arteries.—Aneurism.*

§ 223. Attempts to introduce order among the infinite variety of forms presented by true aneurisms, *i.e.* aneurisms involving all the three arterial coats, used at one time to be based on the shape of the dilated vessels as a *fundamentum divisionis;* this led to the distinction of cylindrical, saccular, fusiform and varicose aneurisms. These attempts all failed. We should be more successful could we make use of the etiology, the mode of origin of the various aneurisms, as a clue to the diversity of the individual forms. But the etiology of aneurism is unfortunately very obscure; and it may be long before it is finally cleared up. Hypotheses indeed abound. *E.g.* nothing seems more tempting than to seek for the origin of the mischief in a lack of elasticity or of contractile power in the muscular coat. Of all the component elements of the arterial wall the muscular fibres are those in which nutritive change is most active, and which, we may fairly assume, are most susceptible of nutritive disturbance. Hence I willingly take refuge in the hypothesis of atony of the middle coat, to explain the uniform cylindrical or varicose dilatation of all the larger arteries which is frequently met with in old people, without the presence of any visible alteration in their walls. I likewise admit that it may have some, though indeed a less important share in the production of other forms of dilatation. The hypothesis of a simple disturbance of innervation, a paralysis of the muscular coat (*Rokitanski*) is less widely applicable. Here too however there is at least one case in which this explanation commends itself to us. I refer to the anastomotic variety of aneurism. The term denotes a varicose dilatation, elongation and twisting of the trunk and all the branches of an artery—the ectasy of a limited section of the arterial system. It occurs chiefly in the arteries of the scalp, *e.g.* the occipital and temporal arteries, and reminds us too forcibly of that dilatation of the vessels of the head which follows division of the cervical sympathetic, not to suggest a partial disturbance of the vasomotor system as its probable cause. All these however are rare cases, and therefore comparatively unimportant.

§ 224. What is shortly called aneurism at the bed-side—an ectasy confined to a short part of the aorta or some other artery, has its causes shrouded in great obscurity. It is usually complicated with chronic endoarteritis. We must endeavour to ascertain how far this change is capable of contributing to the dilatation of an arterial tube. In the first place, we must reflect that an overgrowth of the intima as such, augments the superficial area as well as the thickness of the inner wall of the vessel. The circumscribed patches of newly-formed connective tissue are not merely superimposed on one another; they likewise penetrate horizontally between the existing lamellæ of the intima, forcing them actively asunder as they grow. We are surely entitled to regard the growth of the inflamed intima in a horizontal plane as at least *one* factor in the dilatation of the vessel. For even though we assign but a small value to its active cooperation, yet we must regard the intima, while it is undergoing the fluctuations of internal change, as less capable of resisting the dilating impulse and increased tension of the blood, than it is in its normal state. I have already pointed out that atheromatous changes in the arterial walls cause a rise in the blood-pressure above and at the affected points of the vascular system. To this must be ascribed in the first place that uniform dilatation of the aorta which is nearly always found in cases of extensive endoarteritis. For the production of a true aneurism however, it is the systolic rise in the blood-pressure which is chiefly important. This differs from that which occurs normally. The diseased condition of the arterial walls hinders that provisional transformation of velocity into elastic tension, which causes the systolic rise in the blood-pressure and its "other mode," velocity, to be distributed over a longer interval of time. Accordingly, both these manifestations of energy culminate at the moment when the systole commences, and collapse immediately afterwards to a proportionate extent. With each ventricular contraction, the diseased artery is subjected to a dilating impulse, to which it can only oppose a passive, not, as before, an active resistance. The patient's throbbing pulse informs us that throughout the whole arterial system, a jerky propulsion of the mass of blood has taken the place of a rhythmic acceleration of its current. The brief though forcible shock, which the radial artery communicates to our finger, will be most intense in the aorta itself, since there the loss of energy by way of impact, which necessarily attends this mode of propulsion, does not yet begin to tell. Therefore it is that aneurismal dilatation is most common, first in the ascending aorta; and secondly, wherever the local narrowing of an artery causes a special rise of pressure just behind the obstruction. With special reference to this point, I have examined all the peripheric aneurisms to which I could get access, and I have rarely failed to discover a more or less marked thickening of the intima below the dilated part, as the exciting cause of the lesion. Persistent contraction of those muscles among which the main branches of an artery are distributed, may also cause aneurismal dilatation of the parent-trunk. Thus for example aneurism of the popliteal artery not unfrequently rewards the exertions of those lackeys who stand for hours together behind their masters' carriages (contraction of gastrocnemii).

§ 225. As regards the outward form of aneurisms, the uniformly cylindrical or fusiform dilatation of the arterial tube is usually distinguished from the one-sided, saccular protrusion of its coats. The cylindrical aneurism becomes an invaginating one when the aneurismal sac, at one or both of its extremities, overlaps the corresponding ends of the undilated part of the vessel. The saccular variety presents similar modifications. Should the sac overlap the parent-vessel on one side only, its cavity is marked off from the interior of the vessel by a projecting semilunar fold; should it overlap its parent-artery both above and below, or on all sides at once, it is said to have "a neck."

Saccular aneurisms, those which project more from the convex than from the concave side of the ascending aorta—are by far the most common. They press from within against the sternum or the sterno-clavicular joint. Aneurisms of the transverse arch also spring more often from the convexity than from the concavity of the vessel. Here too we not unfrequently find aneurisms with narrow necks which ultimately force their way out through the upper aperture of the thorax and invade the œsophagus or the trachea from the front. Aneurisms of the thoracic aorta spring by preference from the back and sides of the vessel and press against the spine. Aneurisms of smaller arteries are much less frequent; among these the most common are aneurisms of the popliteal, carotid and basilar arteries.

§ 226. The most interesting question for the histologist is that concerning the behaviour of the various structural components of the arterial tube during its gradual dilatation—the behaviour of the inner, middle and outer coats respectively.

Attention has already been drawn to the fact that the *intima* is usually thickened by previous endoarteritis. This enables it to take part in the dilatation without becoming notably thinner. Aneurisms from four to six inches in diameter may be lined with an internal coat of normal thickness; nay, of more than normal thickness in parts. It exhibits the most diverse stages of atheromatous degeneration side by side; foremost among them however stands calcification; calcified plates have been found involving one-half or even the whole of the circumference of the aneurism, converting it into a bony drum. More common is a tesselated mosaic of smaller plates, which are very liable to become detached at their edges, and so to give the first impulse to the formation of coagula. Fatty degeneration, though less widely distributed, is nevertheless of the utmost moment. For it is this—particularly when it results in the production of atheromatous ulcers—which ultimately leads to perforation of the intima at some point or other, and so exposes the integrity of the sac to the most serious risks.

From the first outset of dilatation the *middle coat* remains entirely passive. The transverse bundles of smooth muscular fibres separate from one another and allow ever-widening fissures to gape between them. They finally succumb to fatty degeneration. Even when an aortic aneurism is no bigger than the closed fist, it is a difficult matter to find any vestige or remnant of the middle coat in its walls.

On the other hand the *adventitia* may be said, in the strictest sense of the word, to "guarantee the sac against rupture." The pressure of the growing aneurism acts upon this membrane in just the same way as a gradually increasing or oft-recurring pressure acts upon a stratum of unformed connective tissue elsewhere; it stimulates it to a chronic inflammatory, or in other words, to a reactive overgrowth. The aneurism comes to be invested on all sides by a close web of tough connective tissue, which supplies whatever deficiencies there may be in the inner coats, and serves as a bond of union between the outer surface of the aneurism and the neighbouring organs.

The implication of the adventitia in the morbid process is therefore wholly salutary. Its resources however are not inexhaustible. First, it cannot, whatever may be its thickness, arrest the growth of the aneurism. It yields uniformly and at all points to the centrifugal pressure of the blood, and can never offer anything like the resistance which is opposed by the combined strength of a healthy internal and middle coat. Some notion of the demands made upon the resisting power of the aneurismal walls may be got by observing the conflict of an aneurism with the osseous system. Should an aneurism of the ascending aorta press forwards against the sternum, or one of the thoracic aorta against the spine, it begins by destroying whatever structures may intervene between the blood and the bone. Intima, media and adventitia, mediastinal connective tissue and periosteum, disappear without leaving any trace, under the stress of the contending forces. Next, the bone begins to yield; it yields slowly—so that denuded remnants of it are often found projecting far into the sac—but still it yields and is absorbed. The bone-tissue under these circumstances passes through a peculiar fibroid metamorphosis (fig. 11) which has been more fully described in § 41. This however can only be regarded as a passing phase in its disintegration and liquefaction. The result is a loss of substance in the bone. Aneurisms of the ascending aorta often annihilate the whole of the manubrium, the upper part of the body of the sternum, and the sternal end of the clavicle. Aneurisms of the descending aorta excavate cup-shaped hollows in the bodies of one or more of the vertebræ.

Another hindrance to the conservative powers of the adventitia arises from the circumstance that these powers, which depend in great measure upon the transfer of hyperplastic activity to the neighbouring connective tissue, have the extent of their operation limited by the extent of distribution of that connective tissue. Every free surface which the aneurism approaches may be fatal to the patient, inasmuch as it gives the aneurism an opportunity of bursting. The pleural surface is the least dangerous in this respect; for the pleural sac is merely an interstice in the connective tissue, whose opposed surfaces readily cohere. The pressure of the aneurism is thus transferred to the lung, and the fatal issue is for a time delayed. It cannot take place till both of the pleural laminæ have been perforated and the spongy parenchyma with the smaller bronchi laid open in consequence. Those aneurisms which force their way towards the larger bronchi or the trachea itself burst at a much earlier period. Aneurisms of the ascending aorta ultimately burst through the skin; rupture may also occur into the œsophagus, pericardium or pulmonary artery; more rarely, into the peritoneum or the retro-peritoneal connective tissue.

§ 227. Clots often form in the cavity of the aneurism. The first impulse to their formation is usually given by irregularities of the internal surface. Retardation of the blood-current is also an important factor; hence the peculiar frequency with which the blood coagulates in saccular aneurisms with narrow necks. These aneurismal thrombi are always exquisitely laminated; the outer layers, those first deposited, are usually quite decolorised, tough and fibrous, like all clots which have been exposed to continued pressure; no trace of commencing organisation can ever be detected. Hence it is that the formation of thrombi in an aneurism, though directly lessening the size of its cavity, seldom leads to a spontaneous cure. This has only been known to occur in aneurisms of small arteries which have been quite shut off from the parent-vessel. For the most part, the filling-up of an aneurismal sac with coagula proves inadequate to resist the impulse of the blood. Should the sac burst, the thrombus is torn up and the blood forces its way out between its fragments. Aneurismal coagula may also undergo softening, an event which facilitates the detachment of fragments and increases the risk of embolism.

β. *Dilatation of Veins.—Phlebectasy.*

§ 228. Dilatations of veins, notwithstanding their greater frequency, notwithstanding the many anatomical peculiarities which they present, are but a feeble copy of arterial dilatations. It has been already stated that an "endophlebitis chronica," analogous to atheromatous disease of the arteries, can hardly be said to exist. This at once does away with the complication which played so weighty a part in the causation of aneurism. The etiology of phlebectasy is obviously one and the same in all cases, *sc.* mechanical dilatation in consequence of a local rise in the blood-pressure; and to this etiological monotony corresponds an equal uniformity in the course of the anatomical alterations. It is quite possible to find in dilatations of the veins the three main forms which may result from the distension of a cylindrical tube; we may distinguish between cylindrical, fusiform and saccular phlebectasy; but such distinctions are here of trifling value, simply because in most cases of phlebectasy all three varieties coëxist; indeed the disorder is never restricted to a single and very marked dilatation of a vein, but always involves the moderate dilatation of an entire plexus, or of all the branches of a single trunk.

Under normal conditions the pressure of the blood in the venous system is so insignificant, that in the larger veins it barely exceeds that of the atmosphere, and may even fall below it in the immediate neighbourhood of the heart. Accordingly, the walls of the veins are comparatively thin; they are, so to say, only adapted to resist this moderate degree of pressure. Should any circumstance raise the blood-pressure, the calibre of the vein must necessarily increase, and its walls be put on the stretch; if the increased pressure continue, or even if it recur periodically, the walls of the vein become permanently distended, and phlebectasy is the result.

§ 229. Phlebectasy, as might be supposed, begins in the immediate neighbourhood of the valves. The sinuses just above the valves are distended, and form small, nodular varicosities along the vein; its superficial position enables them to be readily distinguished through the skin. The valve-flaps themselves have to support a greater weight than usual; they finally become incompetent, and the greater their incompetence, the farther does the ectasy extend along the vein. At first, the vein is stretched longitudinally; inasmuch however as it is fixed at both ends and cannot be sufficiently displaced, the elongated vessel must either bend from side to side, forming zigzags, or become spirally twisted. Both varieties occur, the zigzag in the larger, the spiral in the smaller veins. The former serves as a transition to that degree of phlebectasy which we call "varicosity." The convexity of the curve bulges more than its concavity, and a saccular dilatation is the result, appended to the vein just as a saccular aneurism is appended to an artery. Supposing this process to be repeated at every fresh curve which the vessel makes, the vein must come at last to appear as though it were entirely made up of an alternating series of saccular aneurisms. This is the fully-developed "varicose state" which is usually found involving all the veins of a plexus, or the collective radicles of a large venous trunk. This is usually the point at which phlebectasy culminates. Only the "varicose tumour" can fairly be put higher; and this is confined to one particular locality, namely the hæmorrhoidal plexus.

§ 230. The venous plexuses of the true pelvis and its outlet stand foremost among the veins of the body in their tendency to become dilated. This is partly owing to their anastomotic connexions with the portal vein (Vena hæmorrhoidalis interna), which render them liable to all those influences which interfere with the portal circulation, without conferring any of the compensatory advantages accruing to the latter from intra-abdominal pressure; another cause may be sought in the frequent and prolonged congestion to which these parts are exposed during the performance of the sexual functions. Varicosity of the vesical plexus underlies those morbid changes about the neck of the bladder (catarrh of the mucous membrane, moderate enlargement of the prostate) which are so common in old people, and are usually known as hæmorrhoids of the bladder.

Dilatation of the hæmorrhoidal plexus (true hæmorrhoids) begins with congestion of the venous radicles in the lax submucous tissue of the rectum close to the anus. This is speedily associated with a mucous catarrh of the surface, and, as I myself have found, with a trifling overgrowth of the mucous follicles. At a later stage, the changes in the mucous membrane recede, and the phlebectasy proceeds to the development of large plexuses of varicose veins which push the mucous membrane before them, and form a ring of transverse rugæ round the anal aperture. The dilatation finally concentrates itself at one or more points of these rugæ, which develope into rounded protuberances, and ultimately into fungoid tumours of considerable size.

If we cut through a large hæmorrhoidal nodule, we may see, even without a microscope, that the chief part of its texture is spongy. The pores correspond to the lumina, the septa to the fused walls of those veins which have undergone dilatation and varicose degeneration. We must suppose the structure in question to be produced by atrophy of the interstitial connective tissue; this wastes under the pressure of the distended veins, which is kept up by the persistently increased tension of the blood in their interior; so that, after a time, nothing is left save only the walls of the veins themselves. Inflammatory action is often set up about these venous plexuses; it may either result in induration or in suppuration. The blood may coagulate here and there in their interior, causing partial gangrene.

§ 231. Next to the veins of the pelvic viscera, phlebectasy most frequently affects the branches of the great saphena. Any circumstance which retards the flow of blood through the common iliac vein—as *e.g.* the pressure of the gravid womb or of a pelvic tumour—may give rise to this accident. It may also be caused by prolonged contraction of the muscles of the leg, as *e.g.* in persons who have to work standing; the muscular contraction, by compressing the deeper veins of the leg, drives the blood into the subcutaneous channels. Then gravity helps. Generally speaking, dilatation of the saphena is due to the co-operation of several distinct factors. Its various stages may be followed even through the overlying skin. In its milder as well as its more severe forms, it often underlies those chronic inflammatory and ulcerative disorders of the lower limbs, whose obstinacy so often exposes the temper of both physician and patient to severe trials.

γ. *Dilatation of Capillaries.—Telengiectasis.*

§ 232. Apart from the more or less transitory dilatation consequent on hyperæmia, there is really no condition of the capillary vessels which can be compared to aneurism or phlebectasy. The disorder specifically termed "telengiectasis" consists in an over-production of capillaries in circumscribed portions of the skin. The parenchyma of many organs, among others that of the skin and its proximate constituents, the papillæ, glands, clusters of fat-cells, &c., is primarily divided into territories by that system of anastomosing lacunæ in the connective tissue, whose nodal points contain the connective-tissue corpuscles. The thick protoplasmic processes of these corpuscles map out the course of the new vessels in the tertiary mode of vascularisation (*see Kölliker*, Handbuch d. Gewebelehre, 3te Auflage, page 607). They describe curves of variable radius, which rest at each end upon the wall of an already pervious capillary. The lumen of the new capillary is opened up along this curve. The thread of protoplasm forms a thin coating over the whole of its internal surface, and hardens into a homogeneous capillary membrane; the nuclei of the cells which take part in the process, are shifted, together with the residual protoplasm, to the outer surface of the membrane, where they figure henceforward as "capillary nuclei."

During the vascularisation of growing organs, only a small proportion of the existing connective-tissue corpuscles is usually employed in the formation of vessels. Matters take a different course in telengiectasis. This is due to an enormous excess in the development of connecting channels between the main capillary loops, operated in the manner I have just described. Telengiectasis therefore is an overgrowth, not a mere dilatation of the vessels. The cluster of fat-cells, the sebaceous gland, the sweat-gland, the cutaneous papilla, are permeated by an enormous number of very fine capillaries (which are for the most part spirally contorted) in place of the usual network of connective-tissue corpuscles. All the above structures may be recognised in the innumerable lobules of which the telengiectatic part consists, even should their specific elements have been destroyed by the pressure of those very vessels which were destined for their nourishment.

The dilatation of the capillaries in the growth of cavernous tumours has already been described (§ 129).

2. Diseases of the Heart.

§ 233. In the central organ of the circulatory system we find the same three layers of which the walls of all the greater vessels are made up. The endocardium corresponds to the intima, the myocardium to the middle coat, the pericardium to the adventitia. In harmony with the functional superiority of the heart however, each of these three layers is more highly developed, and that in a direction peculiar to itself.

The endocardium is a far more delicate membrane than the internal coat of the aorta. This is especially well seen on the inner surface of the ventricles, where it appears simply as a lustrous surface, limiting the muscular layer internally, but not in any way affecting either its colour or its modelling. Where it forms duplicatures in which strength is especially required—*sc.* the valves and chordae tendineæ—it becomes thicker. In the valves indeed we find the endocardium made up of several distinct layers. Thus the lamella of each valve-flap which is turned away from the blood-current contains a larger proportion of elastic fibres than that which is turned towards it, and between the two lamellæ, at least in the mitral and tricuspid valves, there is a thin layer of loose connective tissue in which vessels run nearly as far as the edge of the valve.

The myocardium is the thickest of the three layers of which the heart's wall consists, as might be anticipated from its functional importance; its structure affords a solution of the difficult problem, how to enclose a cavity with striped muscular fibre. The fibres anastomose with one another at acute angles, forming fenestrated membranes; and these, lying one upon another in massive strata, and firmly united among themselves, enclose the cavity (cf. § 235, fig. 85).

The adventitia reappears as a serous sac, the pericardium, whose visceral layer invests the outer surface of the heart with a membrane quite as thin as the endocardium upon its inner surface. It nevertheless contains vessels of its own, although they anastomose at many points with those of the muscular substance.

The above remarks all tend to show that the three layers of which the wall of the heart consists, are more specialised, more independent, than the corresponding structures in the arteries and veins; and since this increased specialisation makes itself felt in the diseases to which they are liable, it must be borne in mind throughout the whole of the ensuing discussion. Accordingly, the pathological histology of the myocardium and endocardium will be treated successively, that of the pericardium being relegated to the general chapter which will be devoted to the morbid anatomy of serous membranes.

α. MYOCARDIUM.

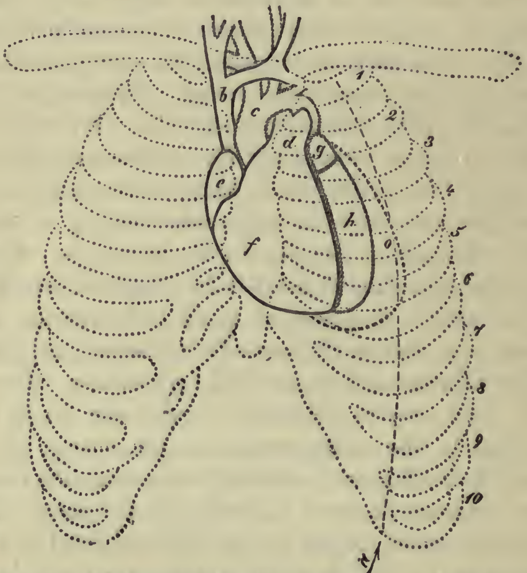
A. *Hypertrophy of the Heart.*

§ 234. By hypertrophy of the heart we understand an increase in the bulk of that organ, due to overgrowth of its muscular coat. It may affect both ventricles equally; it more often affects one only, or chiefly. It is not an easy matter to ascertain the existence of a moderate degree of hypertrophy. We are told to compare the thickness of the walls with the size of the cavity. But their ratio varies with every variation in the degree to which the heart is contracted. The size of the cavity varies inversely as the thickness of its walls. We are never sure whether the seeming increase in the thickness of the wall may not be merely due to the heart being more firmly contracted. Doubts of this sort meet us again when we try to find out if the heart's substance is atrophied; we have to be on our guard against supposing a dilated heart to be atrophied merely because its walls are thin. A power of quick and accurate judgment with regard to moderate degrees of thickening and thinning of the heart's walls can only be got by long practice. On the other hand it is very easy to recognise hypertrophy in its extremer forms. Next to the enlargement and the change in shape—a change which is often very striking—our attention is roused by the disproportionate increase in weight of the heart. The walls of the hypertrophied organ are as stiff and hard as boards, so that even after the blood has been entirely evacuated by incision, they do not collapse, and cannot be easily bent in or out. Finally, the marked increase in thickness of the wall is made all the more striking by the coincident enlargement of the cavity, since hypertrophy is invariably associated with a certain degree of dilatation. A large heart must needs have a large cavity.

The shape of the heart is characteristically altered when only one of the two ventricles is hypertrophied. If we were to join the left ventricle of an adult to the right ventricle of an infant, the entire heart would appear to consist chiefly of the left ventricle; reversing the process, the right ventricle would preponderate in like manner. This exactly illustrates what happens in unilateral hypertrophy of the heart.

A heart with a hypertrophied *left ventricle* (fig. 83) will therefore present an ovate or barrel-shaped outline. The right ventricle appears even more than is usually the case, to be a mere appendage of the left. The long axis of the heart becomes more horizontal, so that the base is turned to the right side, the apex to the left. The apex is pushed beyond the mammary line, as may be ascertained by the extension of the cardiac dulness in this direction and the dislocation of the apex-beat.

FIG. 83.

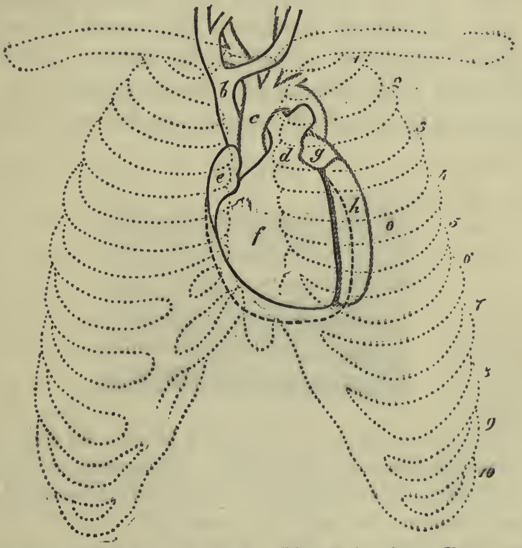


Hypertrophy of left ventricle. Heart *in situ*. *a*. Left mammary line; *b*. V. cava superior; *c*. Aorta; *d*. Bulb of pulmonary artery; *e*. Right auricle; *f*. Right ventricle; *g*. Left auricle; *h*. Left ventricle (normal size); *o*. Left ventricle (hypertrophied).

On the other hand, a one-sided hypertrophy of the *right ventricle* (fig. 84) occasions, not an elongation, but a widening and thickening of the entire heart. Looked at in front, the heart appears square, and as its long axis tends more and more to become vertical, the cardiac dulness extends to the right, presents itself over the lower part of the sternum, and stretches across the right border of that bone. The heart's apex is no longer formed by the left ventricle alone; it is partly, or even wholly formed by the right one. The apex-beat often becomes indistinct; in its stead we find a basic impulse due to the contact of the *conus arteriosus* (fig. 84, *d*) with the chest-wall during each systole, in consequence of the enlargement of the base of the heart in its antero-posterior diameter.

§ 235. Hypertrophy of the heart is invariably due to overwork; it is caused by mechanical hindrances to the onward flow of the blood. These increase the labour of the heart by augmenting the pressure which at the beginning of each systole acts vertically against the inner surface of the ventricle, and which has to be overcome by its contraction. We have already seen hypertrophy of the left ventricle associated with atheromatous degeneration of the aorta; we shall soon become acquainted with lesions of the cardiac valves as by far the commonest causes of hypertrophy, and we shall find ourselves obliged to refer to the subject again and again in discussing other organic diseases. As regards the histological details of hypertrophy of the muscular substance of the heart, the hypothesis that the

FIG. 84.

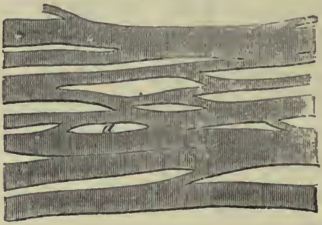


Hypertrophy of right ventricle. Heart *in situ.* References as in previous figure. The dotted line represents the outline of the hypertrophied right ventricle.

individual fibres grow thicker, is very generally received. Nevertheless, I have failed to discover any difference in the thickness of the muscular fibres of hypertrophied hearts; so that I have at last been led to assume that a "partial splitting" of the fibres must occur; an assumption which can only be admitted as regards the heart.

The muscular fibres of the heart, as every one is aware, divide dichotomously; they may also be said to reunite in the same way, forming networks or membranes with elongated, slit-like meshes. These meshes vary greatly in their size; large, spindle-shaped lacunæ alternating with slits and fissures of the smallest size. Some of the latter may even be regarded as situated in the substance of individual fibres. They are most frequently found in the thicker fibres, where these give off lateral branches (fig. 85, *a*) and I cannot but believe that the force exerted by the side-branch during its contraction contributes in some measure to the cleavage of the parent-fibre.

Fig. 85.



Network of muscular fibres from the heart. At *a* is an interstice in a muscular fibre, which corresponds in position to the origin of a side branch; by its gradual increase in size, it will add a new mesh to the network.

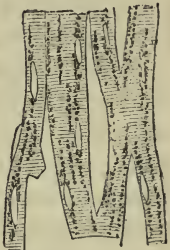
B. *Atrophy of the Heart.*

§ 236. Inasmuch as the heart is undeniably the hardest-working muscle in the body, and therefore consumes more nourishment than most other organs, disturbances in the general nutrition of the organism will necessarily make themselves felt in the heart at a relatively early period. Not only the involution of the body due to old age, but every cachexia, every form of marasmus, whether due to acute or chronic disease, may thus cause wasting of the heart, which manifests itself in thinness and atony of the muscular substance as a whole, and hence as a uniform atrophy of the organ. Besides this general form, we may have partial atrophy—atrophy confined to the outermost or innermost layers of the muscular coat, sometimes indeed limited to circumscribed patches; these partial atrophies being due to local causes.

Whether the change be partial or general, the muscular fibres grow thinner, more slender, and may even disappear entirely. This most important result of atrophy presents itself under variously modified histological forms, which may be classed in as many distinct groups.

§ 237. (1) *Brown atrophy* is characterised, as its anme indicates, by a change in the colour of the muscular tissue, which assumes a rusty-brown or dark ochry hue, coincidently with its diminution in bulk. This peculiar phenomenon is caused by the deposit of a yellow, granular pigment in the interior of the fibres. It may either be uniformly distributed throughout the contractile substance, or the granules may be heaped up in fine lines between the primitive fibrillæ and around the nuclei (fig. 86); their source is unknown; we cannot tell whether they are simply the proper pigment of the muscular fibre condensed, or whether the colouring-matter of the blood has a share in their production. Brown atrophy is always general. It is most common in connexion with senile marasmus, wasting from inanition, the tuberculous and cancerous cachexiæ.

Fig. 86.



Brown atrophy of muscular fibres of the heart. Shred of a muscular layer exhibiting pigment-granules in the interior of the primitive fasciculi. $\frac{1}{300}$.

§ 238. (2) *Yellow atrophy* consists in the transformation of the muscular tissue of the heart into fat. (Cf. § 30 and fig. 7.) In proportion as the deposit of oil-globules is more abundant, the muscular fibres grow pale, then yellowish, and lastly whitish and bacony. They lose their firmness. The tissue grows friable and rotten; it breaks down readily under the finger; on the other hand the loss of bulk is often inconsiderable.

Yellow atrophy contrasts with the brown variety in the rapidity of its development. It presents itself under four forms:

a. As a diffuse degeneration of the entire muscular substance of the heart in the course of acute febrile diseases, the exanthemata, typhus (cf. § 112, *note*), &c.

β. As a fatty disintegration of the superficial, subpericardial layer of the cardiac muscle, in consequence of the nutritive disturbance caused by inflammation of the adjoining pericardium (*see* Pericarditis).

γ. In the form of numerous foci not exceeding a pin's head in size, disseminated through the innermost, subendocardial layer of the muscular substance of such hearts as have been subjected to a high degree of dilatation (valvular insufficiency). In such cases, the whitish dots and striæ due to this affection may be detected even through the endocardium, particularly upon the musculi papillares and columnæ carneæ near the apex.

δ. As a single focus of fatty softening (even as large as a hazel-nut) usually situated in the substance of the wall of the left ventricle near its apex. The atony and friability of the degenerated parenchyma usually cause rupture of the heart, differing from rupture due to other causes by the very gradual manner in which the muscular substance gives way layer after layer. Atheromatous degeneration of the coronary arteries with plugging of one of their larger branches by a thrombus may be regarded in every instance as the cause of this dangerous lesion.

§ 239. *Appendix.* Fatty degeneration of the muscular substance of the heart must not be confounded with that excessive infiltration of the subpericardial connective tissue with fatty matter which is commonly called "fatty heart." The latter is associated with general obesity, and may give rise to very serious troubles, even to death itself. For the masses of fat overgrow the heart from the *sulcus circularis* and *transversus* to such an extent as to conceal the entire surface of each ventricle with the exception of a small patch; it is hardly conceivable that the movements of the heart should not be hindered by so great a burden; then again, the infiltration forces its way into the interstitial connective tissue of the myocardium itself. The latter phenomenon indeed is always confined to a limited patch; the pressure is enough however to cause wasting of the corresponding portion of the heart's wall; and it tends thereby directly to impair the functional powers of the organ.

c. *Inflammation.*

§ 240. Myocarditis is one of the most obscure chapters in general pathology, and morbid anatomy can only contribute very insufficient data for its elucidation. Experience has shown that the most trifling degree of inflammation affecting the striped muscles of the trunk and limbs—*e.g.* even that slight intumescence which we find associated with chronic rheumatism, and with regard to which it is not yet settled whether it really is more than a marked degree of hyperæmia—occasions the most violent disturbances of function. The muscle rests in a state of contraction. Any attempt to extend it is most strenuously opposed by the patient on account of the intense pain to which it gives rise. Now if we apply these results of our experience to the heart, it is obvious from the first that even the most trifling degree of diffuse inflammation ought immediately to be followed by an arrest of the heart's action and the consequent death of the patient, so that the inflammatory process could not attain the later stages of its evolution unless when circumscribed and partial. Some have even gone so far as to deny the possibility of a diffuse myocarditis. Herein they were undoubtedly wrong. I can positively affirm that an inflammation uniformly involving every portion of the heart may exist. A male patient, 54 years of age, who had undergone a protracted course of treatment for constitutional syphilis, and had subsequently passed through an attack of double pneumonia, died suddenly a few days after his discharge from the hospital; his death was so sudden as to rouse suspicions of apoplexy. At the post-mortem examination, apart from some syphilitic lesions, I discovered a condition of the heart which I feel myself justified in unhesitatingly describing as a diffuse parenchymatous inflammation of its muscular substance.

The heart was partially contracted; its walls were so stiff that it could only be compressed by the application of a very large amount of force. Even after the customary incisions had been made into its cavities, its walls did not collapse. At the same time a singular and unusual condition of the muscular tissue excited my attention. It had lost its bright red colour which was dashed with violet; the cut surface was iridescent, its edges nearly transparent; in consistency it resembled caoutchouc;

yet the fibres gave way rather than allow themselves to be stretched. There were numerous ecchymoses under both pericardium and endocardium, which were probably due to great disturbances in the circulation through the muscle; for the vessels were all empty, the lack of blood certainly contributing in some measure to the striking loss of colour.

§ 241. The results of microscopical examination were everywhere the same; the interior of the muscular fibres was occupied by a finely-granular deposit, not uniformly distributed, but forming little fusiform aggregations round the nuclei; it might be regarded as "increased protoplasm." I have never seen a more pregnant illustration of *Virchow's* "parenchymatous inflammation." Moreover the muscular fibres collectively were broken up by transverse clefts into short, oblong fragments, an appearance which is not unusual in the pathological histology of striped muscle. It must always be regarded as due to mechanical rupture. I have assured myself that similar appearances may readily be produced in the muscular fibres of the rabbit by forcible extension. In the present instance we are at no loss to find a cause for such extension, and it may be inferred that the rigid and infiltrated state of the fibres would make them all the more liable to be torn across in this way. It is self-evident also that these minute lacerations must impair the functional power of a muscle quite as much as the most extensive ruptures.

§ 242. Apart from the diffuse, parenchymatous form of myocarditis, certain appearances in the muscular substance of the heart are usually regarded as "results of myocarditis," without our having any adequate knowledge of the chain of phenomena which lead up to them; these are: abscess, and fibroid patch of the heart. The former of these I will describe at once; leaving the latter for the chapter on Chronic Endocarditis.

D. *Abscess of the Heart.*

§ 243. A circumscribed portion of the muscular substance, from the size of a pea to that of a bean, rarely larger than this, but occasionally as big as a walnut—is found to be deficient; its place is taken by a tolerably thick pulp of a yellowish-grey or dirty-grey colour. This pulp consists, apart from numerous pus-corpuscles, mainly of the *débris* of disintegrated muscular fibres, albuminoid molecules, and oil-globules; it also contains larger shreds of the contractile tissue, in which, however, the transverse striation is no longer to be recognised. The affected part is, in the main, of oval form; but sinuses burrowing far into the muscular layer are also occasionally met with. The boundary of the deposit sometimes consists of a very soft layer of reddish-grey material—granulation-tissue, according to *Rokitanski.* Should the abscess approach the endocardium, it may peel it off; sometimes too, it forces its way between the lamellæ of the cuspid valves.

§ 244. This condition may terminate in various ways. In very rare cases, the purulent pulp may become inspissated into a cheesy mass, and surround itself with a capsule of connective tissue; the cheesy nodule ultimately becoming calcareous and establishing a toleration of its presence. More commonly the abscess bursts, and its contents escape. According as it approaches the outer or the inner surface of the myocardium, it bursts either into the pericardial sac, setting up a rapidly fatal pericarditis, or into one of the cavities of the heart itself. In the latter event the bursting of the abscess is immediately followed by a rush of blood into its cavity which washes out the contained *débris.* This opens out wide contingencies of embolism, mainly in the region of the systemic circulation, inasmuch as the abscess is usually situated in the wall of the left ventricle. The abscess-cavity becomes a diverticulum, or an aneurism of the heart's cavities, if the name be preferred. (Acute aneurism of the heart.) How long this state of things may last, depends entirely on the thickness of the hitherto unaffected portion of the wall of the heart. For it is this alone, together with the visceral layer of the pericardium, which delays the inevitable rupture of the heart and the fatal extravasation of blood into the pericardial sac. When the abscess, as often happens, is situated in the septum ventriculorum, the result is somewhat different. A communication between the ventricular cavities by a small opening does not seem to have any marked influence upon the circulation; should the suppurative change however have extended upwards from the septum, should the pus have burrowed into the lax connective tissue between the lamellæ of the tricuspid valve, the bursting of the abscess may cause detachment of all the three flaps which are attached to the septum, *sc.* the inner curtain of the tricuspid, the left flap of the pulmonary and the right flap of the aortic valves; the result of course being insufficiency of the corresponding valvular apparatus (cf. incompetence and stenosis of the valvular apertures of the heart, § 255).

§ 245. *Appendix.* The term "abscess of the heart," besides being applied to the large solitary lesion described above, is also employed to denote those small and scattered foci of softening, not exceeding a pin's head in size, which are occasionally found in connexion with pyæmic, puerperal, glanderous and other forms of blood-poisoning, and which are always multiple. Some of them are usually situated immediately beneath the endo- or pericardium. They make their first appearance as greyish specks in the muscular tissue; later, as minute cavities filled with a diffluent pulp. No true pus-corpuscles can be detected under the microscope, nothing indeed but vibrios (*see* § 24). At first, these vibrios are found packed closely between the muscular fasciculi; they subsequently penetrate into their interior, the muscular fibres simultaneously undergoing disintegration; in fact, transverse sections give one the impression that the contractile substance is actually breaking up into vibrios, since the substitution of a mass of vibrios for the muscular fibre takes place without any increase in its volume. The alterations do not admit of being traced beyond the formation of little abscess-like foci of softening, inasmuch as the affection occurs exclusively in the most violent and quickly fatal forms of the said toxæmic disorders.

E. *Heteroplastic Tumours of the Heart.*

§ 246. When we come to consider the morbid anatomy of serous membranes we shall become acquainted with a primary sarcoma of the pericardium. Apart from this, all cancerous, tuberculous, and sarcomatous affections of the heart are of metastatic origin. But even these are rare. The occurrence of *miliary tubercles* in the heart has only been known within the last few years. *Recklinghausen* discovered them in the muscular tissue of that organ; indeed it is a general rule that all heteroplastic growths are principally met with in the connective tissue of the myocardium. I have recently met twice with miliary tubercles in the endocardium, near the free border of the mitral valve.

Both cases occurred in children, in connexion with acute miliary tuberculosis of all the serous membranes and the pia mater.

§ 247. The large cheesy nodules in the myocardium which used formerly to be called "tubercles of the heart" are in all probability, as *Virchow* has recently shown, not tuberculous but syphilitic.

Gummata of the heart are most commonly found in the septum between the ventricles. As a general rule, several nodules not larger than a pea are held together by a quantity of inflammatory connective tissue, forming a single tuberculated mass; we do however find solitary nodules of so remarkable a size, that they protrude into the cavity of both ventricles at once.

§ 248. *Cancerous* nodules—secondary to medullary or melanotic growths elsewhere—seldom grow to any size in the heart. We rarely find them larger than a hazel-nut. They all originate in the connective tissue of the myocardium, and force their way, according to their position, either inwards or outwards; in the former case, they detach and occasionally perforate the endocardium, in the latter, they do the same to the pericardium. It has also been asserted that thrombi of the heart's cavities (polypi of the heart) are susceptible of undergoing cancerous degeneration; but this assertion is grievously in need of being corroborated.

β. ENDOCARDIUM.

A. *Acute Endocarditis.*

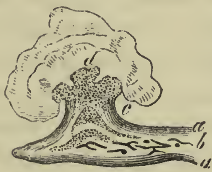
§ 249. Attention has already been drawn to the fact that the endocardium, although the analogue of the internal coat of the vessels, is yet far more delicate in its texture; that it contains vessels—at least here and there; that where these are lacking, the rich vascular network of the myocardium sends its terminal loops close under the thin lining membrane, so that we may regard the latter as standing in direct connexion with the *vasa vasorum*. We cannot therefore be surprised to find that the endocardium is far more susceptible than the tunica intima of the vessels. Various anomalies in the composition of the blood, the pyæmic, puerperal and typhous dyscrasiæ—but above all, the dyscrasia associated with acute articular rheumatism, act as inflammatory irritants upon the endocardium. According to *Bamberger's* estimate, 20°/₀ of all the cases of acute articular rheumatism are complicated with endocarditis.

As regards the more precise localisation of the process, we must first call attention to the fact, that the endocardial lining of the left heart is so preeminently liable to become affected that cases of endocarditis of the right heart belong to the curiosities of pathology. Next, there is a marked connexion between the seat of the disease and the mechanical irritation to which certain regions of the endocardial surface are exposed during the heart's contractions. Such are the lines along which the valve-flaps come into contact during their closure; not the free edges of the valves, but lines which even in the normal state are very apparent on the sigmoid valves, lines which coincide with the free border of each flap only at its middle point (nodulus Arantii) and at its two extremities, but which are separated from it elsewhere by an interval of from half a line to one line; on the cuspid valves the "line of contact" is everywhere one line off the free border; it runs along the upper surface of each flap, corresponding exactly to the insertion of the upper ends of the forked chordæ tendineæ upon its inferior or ventricular aspect. It is here as a rule that we must seek for the earliest signs of morbid change. Starting from hence, the mischief may extend over a great part of the valve; it may burst forth simultaneously at another point of the endocardial surface; but the "lines of contact" of the valves are and continue to be its favourite seat.

§ 250. The textural change in acute endocarditis is made up of three factors of very unequal value. In the first place, an implication of the *vasa vasorum* may be demonstrated wherever they happen to run in the neighbourhood of the inflamed part. Congestion and a considerable proliferation of the corpuscular elements of the adventitia may always be shown in transverse sections through the inflamed curtains of the mitral valve (fig. 87, *b*). Of far greater moment are the progressive changes which take place in the non-vascular, most superficial lamellæ of the endocardium. Their connective tissue, owing to the proliferation of young cells in large numbers and a simultaneous softening of the intercellular substance, swells up to such an extent, that even with the naked eye we can detect a series of warty prominences on the surface of the valve (fig. 87, *c*).

These granulations are exceedingly frail. Not only does their mutual contact during the closure of the valves splinter and damage their soft tissues, but they speedily fall a prey to a finely-granular, not fatty, metamorphosis of their entire substance; this renders the vegetation so very brittle, that the blood-current easily washes large and small bits of it away. When this happens, a proportionate loss of substance, the "endocarditic ulcer," is produced, which usually penetrates clean through one lamella of the valve. The edges of the ulcer are always irregularly raised; they exhibit, so long as the endocarditis is on the increase, the primary stages of the process, which extends to the neighbouring connective tissue. A similar extension occurs, though less frequently, at the base of the ulcer; the remaining lamella of the curtain becomes involved, and when this yields the valve is perforated. Perforation of a valve is one of the most dangerous accidents that can happen; for the force of the blood-current may easily dilate the original opening; or the curtain may be detached on one or other side. In the cuspid valves, it occasionally happens that the whole edge of the curtain is detached together with the insertions of the musculi papillares. The perforation, like the ulcer, is invariably fringed with the inflammatory vegetations described above, which, in consequence of the fibrinous deposit of which I am now about to speak, may assume so great a size, that the opening in their midst can hardly be detected.

Fig. 87.



Acute endocarditis. Section through one of the curtains of the inflamed mitral valve. *a*. Upper, *a'*. lower lamella of the endocardium; *b*. Intermediate layer, whose vessels are congested; *c*. Efflorescence of upper lamella; *d*. Deposit of fibrin. $\frac{1}{10}$.

This rapid course of endocarditis in its most usual form never issues in suppuration. This is anticipated by the granular disintegration alluded to above—a sort of necrosis of the newly-formed substance. This must not be taken to mean that suppuration *never* complicates the morbid anatomy of endocarditis. Only, when pus is formed, it is always confined to the loose connective tissue between the lamellæ of the valves, and to the subendocardial connective tissue; moreover it never collects in any quantity, but always takes the form of minute abscesses, no bigger than a pin's head, which cause pustular elevations of the endocardium.

The third factor which plays a more or less conspicuous part in every case of acute endocarditis, is the precipitation of fibrin upon the roughened surface of the affected valve. I lay stress on the fact that fibrin alone is usually deposited; the thrombus rarely contains any red corpuscles. I cannot help thinking that owing to the naked-eye resemblance of the fibrinous deposit to the proper outgrowth from the tissue, their real distinctness is often overlooked. The precipitated fibrin (fig. 87, *d*) fills up all the little inequalities of the surface, and increases the total bulk of the efflorescence to such a disproportionate extent, that it strikes the observer much more forcibly than the morbid change in the valve itself. To conclude: the coagulation of the fibrin is not, any more than in an aneurism, to be regarded as a salutary phenomenon, as a first step towards recovery. The fibrin readily becomes disintegrated. It does not therefore operate as a check either to the progress of the ulceration, or to the perforation of the valve, while it enhances the risk of metastatic inflammations consequent on embolism of its detached fragments.

B. *Valvular Aneurism.*

§ 251. The way in which the so-called valvular aneurism originates, is worthy of particular notice. Under this name—taken broadly—we understand any circumscribed bulging in the continuity of a valve. Conditions of this sort are not as a rule in any way connected with endocarditis. They are saccular or pouch-like inflexions of a valve, in whose formation both of its lamellæ (without any previous change in their structure) take part. The pouch invariably opens on that side of the valve which is exposed to most pressure when the valve is closed, while the sac itself is on the opposite side. In the aortic valves, we enter the aneurismal sacculus from the sinus of Valsalva; in the cuspid valves, from the ventricular cavity. Besides these, we occasionally meet with diverticula in the walls of the heart, near its orifices, precisely analogous to the aneurisms in question, though a strict use of language must of course forbid us to call them "valvular." These are found at the origin of the coronary arteries and on the floor of the innermost sinus of Valsalva. The latter, by far the most common of these pouches, project into the right heart, sometimes above, sometimes below, sometimes between the lamellæ of that curtain of the tricuspid valve which is attached just opposite to them. The same three paths are open to aneurism of the membranous part of the *septum ventriculorum*, which comes under the present category. It may force its way from the left ventricle, over, under or between the folds of the left curtain of the tricuspid valve, and so into the right ventricle. I have seen a case, in which an aneurism of the sinus of Valsalva, as large as a cherry, projected on the upper surface of that curtain, while on its under surface was one as large as a pea formed by the *septum pellucidum.*

After this digression, let us return to valvular aneurism consequent upon endocarditis. This form is necessarily preceded by the complete destruction of one of the lamellæ of the valve. The blood makes its way into the opening thus produced, forces the lamellæ asunder, and causes a more or less extensive pouching of that which is still intact. The endocarditic or acute valvular aneurism is thus essentially distinguished from the first variety by the fact that the pouch is formed, not by the entire valve, but by one only of its lamellæ.

c. *Perforation of Valves.*

§ 252. Here too we must distinguish between destruction of the valve proper by inflammatory change, and a harmless variety of perforation, which is very often met with at the free borders of the semilunar valves. The latter depends upon a thinning of that portion of the valve which lies *above* the actual "line of contact" (the line along which the valves touch one another during closure), and is in my opinion nothing more than an approximation of the sigmoid to the cuspid type of valve.

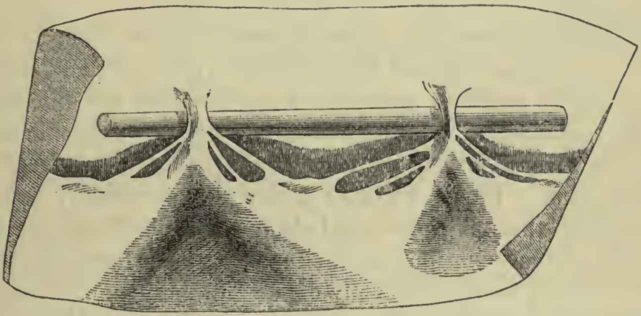
For if we glance at the anatomical arrangements intended to prevent regurgitation of the blood, we see at once that they belong to two distinct types, that of the sigmoid and that of the cuspid valves. This difference of type may be dismissed in a few words. The sigmoid valves are duplicatures of the intima, each of which forms a semicircular fold with its convexity directed towards the current; the terminal points of the lines along which the valves are attached, being all in the same horizontal plane. Accordingly they form pouches, which touch one another by their outer surfaces when they are filled with blood, and so close up the tube. The peculiar way in which these flaps are attached, renders it impossible for them to move otherwise than *with* the current. The cuspid valves on the other hand, consist of moveable curtains, attached in the same horizontal plane, at right angles to the axis of the vessel; and these, so far as their mode of attachment is concerned, might be folded over to either side indifferently; nevertheless, they too can only yield to the blood-current in one direction, inasmuch as the union of their free borders with the chordæ tendineæ prevents their being forced into the cavity of the auricle.

It would indeed be matter for surprise had Nature, usually so simple in the methods she adopts, really contrived two kinds of valve in the present case, differing from one another in principle; we ought therefore to consider whether the apparent diversity of anatomical construction may not be reducible to a simple modification of one and the same fundamental type. Now it seems to me that this type is to be found in the sigmoid form of valve; not only because of its more frequent occurrence in the organism (valves of veins, &c.), but also because the innocuous variety of perforation which we are now considering, presents us with a modification of the sigmoid valve, tending to approximate it to the cuspid type.

This perforation, as may be seen at a glance from the annexed figure, may be regarded as a partial separation of the free border of the valve, extending from the nodulus Arantii to its terminal attachment. Now during the closure of the valves, this free border acts as a retinaculum; it hinders the valve from receding to too great an extent. One need only put the tip of one's forefinger into a sinus of Valsalva, to be convinced that the valvular pouch is narrower at its entrance than at the "line of contact;" *i.e.* that the free margin of the valve forms a shorter and straighter bond between the nodulus Arantii and the wall of the vessel, than does the "line of contact." The free border of the valve therefore acts as a retinaculum in exactly the same way as the chordæ tendineæ of the cuspid valves. For the performance of this function it is clear that all that part of the surface of the valve which lies between the free border and the "line of contact," is superfluous. Hence the disappearance of this intermediate portion (only a few connecting strips of it being left) is an acknowledgment of the functional independence of the free border.

In extreme cases (which are not, upon the whole, rare) of marginal perforation of the valves, a nearer approximation of the sigmoid to the cuspid type is brought about by the existence of an interval between the point at which the marginal part of the valve is attached to the wall of the vessel, and the point at which its "line of contact" is attached. So that the corresponding halves of the free borders of any two contiguous flaps, together with the fine threads which link them with the "line of contact," spring from a point of the arterial wall above the real insertion of the valve. This interval between the points of attachment of the retinacula of the valve-flaps, and that transverse plane of the vessel which it is the business of the valve to close (making it possible to retain the valves in a more vertical, and therefore in a more secure position), is the fundamental principle of the cuspid type of structure. Fig. 88 represents an extreme example of perforation of the sigmoid valves; the bundles of tendinous threads stretched over the glass rod, which

Fig. 88.



Fenestrated semilunar valves from the pulmonary artery. Natural size.

has been passed from one sinus of Valsalva, over the point at which the "line of contact" of the valve springs from the wall of the vessel, into the next sinus, perform the same office as the musculi papillares of the ventricle. The point of origin of the "line of contact" may now be moved further downwards without any uncertainty as to the perfect competency of the valves. The flap itself may become gradually flatter and more pointed, the nodulus Arantii being kept in its old position, while the angle formed by the two limbs of each "line of contact" grows progressively less and less obtuse; this also is well shown by the specimen in the annexed figure. Briefly, the innocuous variety of perforation or fenestration of the sigmoid valves is, in my opinion, a connecting link between the sigmoid and the cuspid types.

D. *Chronic Endocarditis.*

§ 253. In marked contrast to acute inflammation, and that softening of the valvular tissues which results from it, chronic endocarditis produces an extreme condensation and thickening of the endocardium. Most persons suffering from chronic endocarditis give a history of former attacks of acute articular rheumatism. Hence we may admit the possibility, nay the probability, that the endocardial changes may be of acute origin; a lesion, however insignificant, situated in the "line of contact" of the valves, being continually exposed to mechanical irritation, might refuse to heal; and might serve in consequence as a starting-point and centre for a chronic inflammation, such as we often meet with in neglected ulcers of the skin.

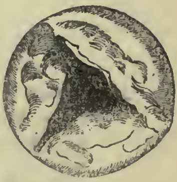
On the other hand, it is necessary to throw the identity of this process with chronic endoarteritis into strong relief. In either case, the microscope shows an inflammatory overgrowth of connective tissue, followed by a secondary stage of calcification, or, more rarely, of fatty degeneration of the newly-formed products. The only special feature about chronic endocarditis is the marked tendency of the inflamed parts to contract. This tendency, of course, can only manifest itself in the duplicatures of the membrane, since their one-sided attachment allows a retraction of their free borders to take place.

§ 254. Every point of the endocardial surface may be the seat of chronic inflammation; yet it affects the valves and the apex of the left ventricle in such an overwhelming majority of cases that I may fairly confine my remarks to these two localities.

E. *Valvular defects.*

§ 255. Those coarser distortions of the orifices of the heart which are caused by chronic endocarditis are embraced under the general head of valvular defects. These are always made up of three distinct anatomical factors, which have to be considered separately in every case: 1. *Thickening*—the immediate result of overgrowth of the connective tissue. Slight degrees of thickening are extremely common at the base of the aortic valves and along the "line of contact" of the mitral; they do not affect the functional activity of the valves. Higher degrees of the same alteration give rise to rough elevations, hardened by earthy deposit; along the "line of contact" of the mitral valve these are usually confined to one surface only; in the aortic valves they usually affect both. They cover the entire surface of the semilunar valves with a layer several lines thick, so that instead of three delicate, sigmoid flaps, we ultimately find three rigid, tuberculated bodies festooned round the wall of the aorta (fig. 89).

Fig. 89.



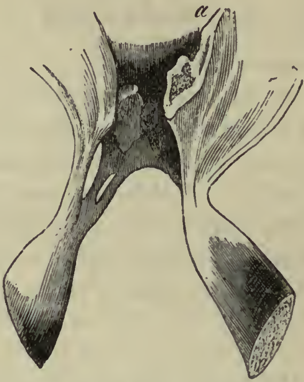
Insufficiency and stenosis of the aortic orifice. Thickening and contraction of the valve-flaps. Natural size.

2. *Retraction.* This results from shrinking of the hyperplastic connective tissue. Together with the thickening, it gives us the impression that the entire mass of the valve is crumpled into a small, elongated roller—that the curtain is rolled up. Curiously enough, the narrow borders of the aortic valve beyond the "line of contact" often remain unaltered, and hang from the free edges of the shrunken valves like flexible bands. At the mitral orifice, where the process extends to the chordæ tendineæ, the shortening causes the valve to be dragged down into the ventricular cavity, thus fixing it in the attitude which it ought only to occupy after the close of each systole (fig. 90).

3. *Adhesion.* The tissue of the inflamed valve, notwithstanding its rigidity, is capable of a certain degree of internal movement; it is in a state of inflammatory fluxion, which allows it to adhere to its fellows, wherever they happen to touch. So long as the valvular apparatus retains its normal mobility, any two

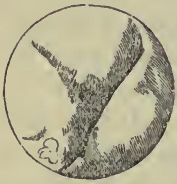
points which touch each other during the closure of the valve, are always separated when it opens; but the inflamed valves no longer, as a rule, possess their full mobility; and adhesion always begins between those points which are least separated during the opening of the valves. The coalescence of two neighbouring flaps takes place along the "line of contact" from without inwards. In the sigmoid valves of the aorta the fusion always occurs first between the right and posterior flaps. When once it has extended as far as the nodulus Arantii, the partition between the adjacent sinuses of Valsalva sinks down, and the two flaps are fused into one; this in some measure does the work of both, unless otherwise prevented by thickening and contraction (fig. 89). Fusion of the curtains of the mitral, stands foremost as regards frequency and mischievous effect. The auriculo-ventricular orifice is thus gradually narrowed from either side, till it finally becomes

FIG. 90.



Insufficiency and stenosis of the mitral valve. The valve is converted into a rigid funnel, laid open at *a*; the musculi papillares have been cut away from the ventricular wall. The cut surface at *a* shows the thickening of the flaps, which is also seen in the background; at *a* moreover there is a nucleus of calcification. The chordæ tendineæ are thickened and fused together; the musc. papillares indurated and tendinous at their tips.

FIG. 91.



Adhesion of the right and posterior flaps of the aortic valve. At *a* the line of union. The valve is competent, though it consists of only two flaps.

a mere slit, the mitral valve forming a rigid diaphragm between the auricle and ventricle. The fusion of the chordæ tendineæ (fig. 90) starts from their points of bifurcation and their oblique insertion into the under surface of the valve. This contributes not a little to the rigidity and immobility of the valve.

Clinical Applications of the above Statements.

It is obvious that the existence of valvular defects must cause profound disturbances, first in the movement of the blood, and secondly in the functions of the various organs. Valvular lesions, whether due to chronic changes or to acute endocarditis, may, from this point of view, be grouped under two heads:

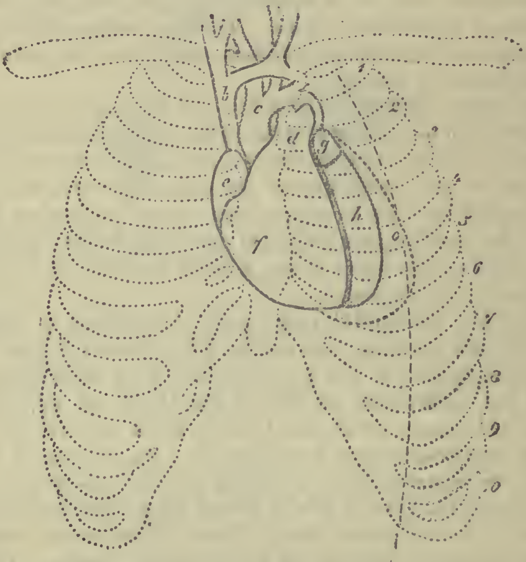
1. Thickening, rigidity, calcification and coalescence of the valves prevent their being accurately applied at the right moment to the wall of the vessel or the ventricle (*sc.* in the case of the aortic valves, during the systole, in that of the mitral, during the diastole), so that the valve continues to project into the corresponding orifice, narrowing its lumen (*stenosis*). The blood-current impinges upon this obstacle and so causes a murmur which is best heard at that point of the thoracic wall, to which it is most directly conducted.

2. Retraction, perforation and partial detachment of valves, and rupture of chordæ tendineæ, prevent the valves from completely closing their respective orifices, at the moment when their tension ought to be opposed to the regurgitant current of the blood; an opening is consequently left, through which the blood returns into the cavity from which it has just been driven (*insufficiency*). The closure of the valves is normally accompanied by two audible sounds; the first, systolic in rhythm, is due to the tension of the mitral valve; the second, diastolic only, to that of the semilunar valves. Now if this sudden tension does not occur, the corresponding sound must also be wanting. In its place we may have a murmur caused by the regurgitation of the blood through the abnormal orifice; a murmur which may indeed be intense, but must always be of short duration. Stenosis and insufficiency always occur together as a result of chronic endocarditis; acute endocarditis, however, by causing perforation and detachment, may be followed by insufficiency without stenosis.

a. Stenosis and Insufficiency of the Aortic Valves (figs. 89 and 92).

The left ventricle of an adult pumps about three ounces of blood (a wineglassful) into the aortic system at each systole. The increased resistance offered by the contracted aortic orifice is transferred as an increase of systolic pressure to the internal surface of the left ventricle, and, according to the law laid down in § 235, must lead to its hypertrophy. At the same time the stenosis will cause a systolic murmur which will be most distinctly heard over the right edge of the sternum on a level with the second intercostal space, inasmuch as the ascending limb of the aortic arch lies in close proximity to the thoracic wall at this point (fig. 92, *c*). The murmur is propagated into the arteries. Another series of phenomena manifests itself during the diastole of the heart. The insufficiency of the sigmoid valves allows a part of the blood which has just been driven into the aorta to regurgitate, as the pressure in the left ventricle, when it is relaxed, stands lower than that in the aorta. The familiar diastolic click of the healthy valve is no longer heard; its place is taken by a second, diastolic murmur, most clearly heard over the heart's apex towards which the returning blood-current is directed. A farther consequence of the valvular insufficiency is the rapid collapse of the pulse in the arteries; the mechanism of the collapsing pulse in the present case being different from that in chronic endoarteritis. The chief danger which threatens patients suffering from stenosis and insufficiency is undoubtedly the lowering of the blood-pressure in the arteries, and the consequent equalisation of the arterial and venous tension, whose difference alone it is which renders the passage of the blood through the capillaries possible. Hence the blood accumulates in

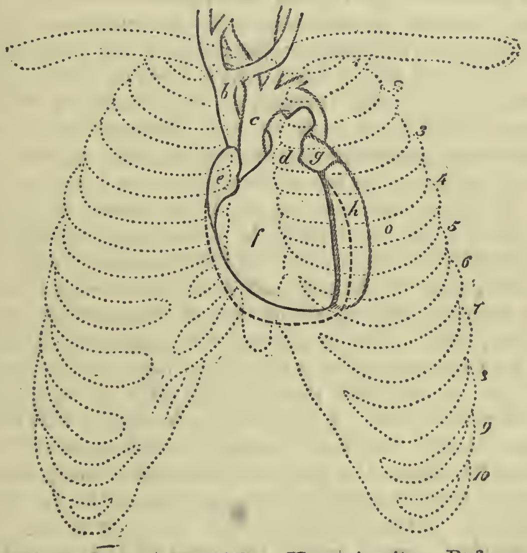
FIG. 92.



Hypertrophy of left ventricle. Heart *in situ*. *a*. Left mammary line; *b*. V. cava superior; *c*. Aorta; *d*. Bulb of pulmonary artery; *e*. Right auricle; *f*. Right ventricle; *g*. Left auricle; *h*. Left ventricle (normal size); *o*. Left ventricle (hypertrophied).

the veins and in the pulmonary circulation, causing cyanosis, dropsy, &c. Meanwhile these extreme symptoms are warded off for a long time by the dilatation of the left heart which accompanies its hypertrophy; this enables it to accommodate an abnormally large amount of blood and adapts it to receive a part of that which has just been driven out of it. This dilatation is a result, not of the insufficiency, but of the stenosis; but it makes amends for the insufficiency just as hypertrophy obviates the dangers of stenosis. All these methods of spontaneous compensation however, have their limits. Supposing the obstruction at the aortic orifice to be complete, it is clear that the utmost degree of hypertrophy and dilatation would not suffice to obviate the imminent fall of tension in the aortic system. Now cases of stenosis occur which are really not far removed from complete occlusion of the aortic orifice.

FIG. 93.



Hypertrophy of right ventricle. Heart *in situ*. References as in previous figure. Dotted line represents outline of hypertrophied right ventricle.

β. Stenosis and Insufficiency of the Mitral Valve (figs. 93 and 90).

Stenosis of the mitral orifice impairs the facility with which the blood normally flows into the left ventricle during the cardiac diastole. The blood stagnates in the left auricle. This stagnation causes a pressure in its interior analogous to the increase of systolic pressure upon the inner surface of the left ventricle in stenosis of the aortic orifice. The left auricle indeed, under such circumstances, is prone to undergo dilatation, which is however, always associated with some thickening both of the muscular coat and the endocardium. A diastolic murmur is naturally generated in the contracted auriculo-ventricular orifice during the cardiac diastole; this is best heard at the heart's apex, towards which the blood-current is directed. Next comes the systole. During this, a portion of the blood which has passed into the ventricle, is driven back into the auricle through the incompetent valve; hence a systolic murmur replacing the first sound, so far as this is due to closure of the mitral valve. In this partial regurgitation of the blood from the left ventricle, we have another cause of increased blood-pressure in the left auricle. So that the insufficiency and the stenosis combine to cause increased tension in the left auricle, and in the whole pulmonary circulation. All the important clinical phenomena group themselves round this as a centre. The increased tension is to some extent salutary, inasmuch as it assists in filling the left ventricle rapidly and completely during the diastole, in spite of the contraction of the mitral orifice. It compensates therefore in some degree for the valvular defect. On the other hand, however, it occasions congestion of the pulmonary vessels, a passive hyperæmia of the lungs, which leads to "brown induration" of those organs (cf. Morbid Anatomy of the Respiratory Organs). The second sound of the heart, so far as it is produced by the pulmonary valves, appears exaggerated, owing to the increased tension of their flaps. This is most distinct to the left of the sternum, on a level with the third rib, where the *conus arteriosus* (fig. 93, *d*) lies nearest to the chest-wall. Again, the work of the right ventricle is increased, inasmuch as it has to open the tightly-stretched valves of the pulmonary artery with each systole, and to pump the blood it contains into the already over-distended pulmonary system. The result of this is hypertrophy of the right ventricle (*see* § 235). The hypertrophy is associated with dilatation. The right auriculo-ventricular orifice takes part in the dilatation, and ultimately gets so wide that the tricuspid valve no longer suffices to close it during the systole. A relative insufficiency of this valve also is thus brought about; the stasis extends to the systemic veins, and leads to morbid changes in the liver, alimentary tract, kidneys, &c., which we shall have to consider when we treat of the morbid anatomy of these organs. A highly characteristic symptom of this relative insufficiency of the tricuspid valve is the so-called "venous pulse," due to propagation of the systolic wave into the principal veins. Stenosis with insufficiency of the pulmonary valves is nearly always congenital and will be referred to in the third section of the present chapter. Stenosis with insufficiency of the tricuspid is exceedingly rare. The presence of venous pulsation is one of the chief guides to its recognition.

F. *Fibroid Patch and partial Aneurism of the Heart.*

§ 256. Chronic endocarditis leads to very different results when it invades that part of the endocardium which lines the cavities of the heart. The hyperplastic thickening of the connective-tissue layer in this region, never gives rise to any appreciable elevation of the surface; on the contrary, the affected spot is from the first depressed below the level of the surrounding parts; this depression passes by slow degrees into an actual bulging, and finally into an aneurism.

The anterior wall of the left ventricle is the usual seat of such alterations. Here, in the neighbourhood of the heart's apex, the endocardium assumes a milky, tough, fibroid appearance over a spot as large as a dollar, or even larger. Its surface is smooth; smoother indeed than it ought to be; we miss the irregular conformation which this region in particular owes to the columnæ carneæ. On cutting into it we find that underneath the thickened endocardium not only the columnæ carneæ, but the entire muscular coat has disappeared. We find a "tendinous spot" extending through the entire thickness of the heart's wall, from one to two lines thick, made up of white, dense, inelastic connective tissue; in it we are no longer able to distinguish endocardium from muscle, muscle from pericardium. Under these circumstances it becomes a question, whether the entire process is not to be regarded as essentially a circumscribed indurative inflammation of the muscular tissue (§ 242). There can be no doubt that the muscular coat of the organ is really destroyed by an overgrowth and shrinking of the interstitial connective tissue. At the edges of the affected part, where the myocardium, growing gradually thinner, passes into the tendinous patch, I have never failed to find atrophied muscular fibres, lost in a connective tissue rich in corpuscular elements, though not in a state of luxuriant proliferation. But I insist that this process must be regarded as a direct extension of the chronic inflammation of the endocardium to the subendocardial and intermuscular connective tissue. For the myocardium is not always utterly annihilated; and it is usually its outer, not its inner layers which still remain intact.

§ 257. The fibroid patch, as I have already said, forms a necessary preliminary to a circumscribed dilatation, a partial aneurism of the heart. Notwithstanding its innate tendency to contract, the newly-formed connective tissue which has taken the place of a portion of the heart's muscular wall is unable to resist the pressure of the blood. The affected patch is accordingly stretched, and assumes the shape either of a uniform, shallow bulging, or of a rounded, saccular appendage to the heart's apex, communicating with the interior of the ventricle by a somewhat narrow opening. The size of the aneurism varies within wide limits, from that of a cherry to that of a hen's egg. Coagulation not unfrequently occurs in its interior; the probability of such a complication being proportionate to the degree in which the aneurism approaches the saccular or pedunculated type. In marked contrast to the aneurismal dilatations of the larger arteries, this form occasionally undergoes spontaneous obliteration; a phenomenon which depends, according to *Rokitanski*, not so much on the presence of a clot, as on the development of vegetations of connective tissue from the inner surface of the sac. Rupture seldom occurs, and only when the walls of the sac are extremely thinned; in striking contrast to its frequency in cases of *acute* aneurism of the heart due to suppurative myocarditis.

G. *Thrombosis of the Heart.—Polypi of the Heart.*

§ 258. If we glance at the usual causes of thrombosis, (roughening of the inner wall of vessels, and retardation of the blood-current) we shall be led *a priori* to the conclusion, that diseases of the heart must afford excellent opportunities for the occurrence of this phenomenon. Attention has already been called to the fact that the recent efflorescences of endocarditis are usually coated with fibrinous deposits of variable thickness; such deposits are very rarely to be seen on the surface of indurated valve-flaps, even when these exhibit projections and irregularities of every sort. We must nevertheless remember that every irregularity of the endocardial surface may serve as a nucleus for the precipitation of fibrin. True, the thrombi so produced are usually of moderate dimensions, and are never converted into those great, globular coagula which are briefly termed "polypi of the heart," or, with *Laennec*, "végétations globuleuses." These are always due to a relative retardation or absolute stoppage of the movement of the blood in certain regions of the heart. The most usual case is that of incomplete expulsion of the blood contained in one or other of the heart's cavities owing to stenosis of an orifice, or to imperfect contraction of the organ. That portion of the contained blood which is farthest from the orifice of exit does not get driven out; it remains in the apex of a ventricle or an auricular appendix as the case may be. In these regions there are a number of pouched recesses, often branched and hidden, from which the blood can never be expelled save by very complete contractions. Such recesses do a great deal to help coagulation; it is in them that we always find the first beginnings of the process. A number of little clots are often found blocking up the intertrabecular spaces of the heart's apex, to such an extent as to fill up, more or less completely, the inequalities which normally exist in that region.

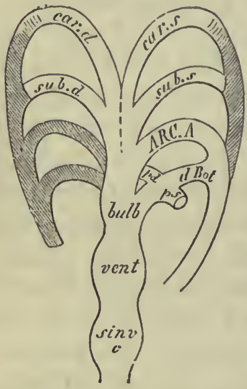
§ 259. The next step is for the various thrombi to protrude from the nooks in which they had their origin; the contiguous ones coalesce; and in this way, simple clots of considerable length and thickness are produced, which take up a great part of the heart's cavities. Their shape conforms in a general way to that of the cavity which they partially fill, and to whose inner surface they are closely applied at each systole. I have seen a thrombus occupying the left auricle project through a contracted mitral orifice (where it exhibited a corresponding contraction) into the left ventricle, where it again swelled out. The clots usually terminate in a rounded end, which led *Laennec* to call them "végétations globuleuses." Their colour depends on the time they have existed. We seldom meet with thrombi of any size which are still solid throughout. Such thrombi exhibit an exquisitely laminated composition, and it is easy to see that this concentric lamination begins in the most external layers of the clot, and that the outermost lamellæ are consequently the oldest.

The farther changes which the thrombus undergoes depend upon the fact that its peripheral layers are better able to obtain nourishment than its nucleus. As a rule therefore, we find decolorisation and softening not in the oldest, but in the most central parts of the entire clot, from which these changes spread, layer by layer, to its surface. They may progress until we have a spherical cyst filled with puriform fluid, attached to the walls of the cavity by solid rootlets (the first intertrabecular coagula). I need hardly add, that if the thrombus should by any chance be broken up, the patient will be in imminent peril of embolism, and the inflammatory and suppurative accidents which flow from embolism.

3. Congenital Malformations of the Circulatory Apparatus.

§ 260. Among congenital malformations of the circulatory apparatus, retarded development of the circulatory system as a whole, in comparison with the remaining parts of the organism, deserves the first place. This shows itself primarily in an abnormal smallness of the heart; the calibre of the aorta and its principal branches being proportionately narrowed and their walls thin. Careful investigation proves that all the smaller arteries and veins are more feebly constructed than they should be. This condition, which principally affects persons of the female sex, is nearly always complicated with corresponding defects in the development of the blood (*see* Chlorosis, § 176), and of the sexual organs; but which of these three sets of deficiencies ought to be regarded as primary, and which as secondary, must remain uncertain. The membranous part of the ventricular septum is deserving of especial notice in these cases, inasmuch as it is usually very large, and predisposed to aneurismal dilatation (§ 251).

Fig. 94.



Diagrammatic representation of the development of the heart and great arterial trunks.

§ 261. A second group of congenital malformations depends on some disturbance of the earliest stages in the development of the heart and great vessels.

Everybody knows that the heart originates as a straight contractile tube in the middle line of the *area germinativa.* This tube presents three dilatations (fig. 94), the *sinus venarum communis*, the ventricle, and the *bulbus aortæ*, besides a number of vascular arches which spring in pairs from the aortic bulb. The shading in the annexed diagram serves to distinguish those of the vascular arches which are ultimately obliterated, from those which remain as permanent trunks; the dotted line indicates that a partition, growing from before backwards, separates the innominate trunk from the left carotid and subclavian. The two latter vessels are then displaced along the aortic arch until they reach the points at which they are given off in the adult animal (fig. 95). That portion of the arch which intervenes between the left subclavian and the *ductus arteriosus Botalli*, is termed the *isthmus aortæ*.

Departures from this order during the early development of the great vessels are not infrequent. Thus the septum between the innominate and left carotid may go beyond the arch, may extend into the aortic bulb. We then get a *double ascending aorta*, whose smaller right limb is nothing but the innominate trunk which has become independent.

Should the separation of the left carotid from the left subclavian remain incomplete, the two vessels spring from a common trunk, a *left innominate artery*.

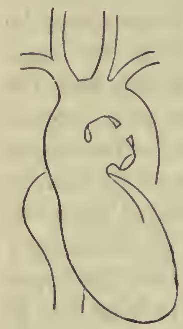
Again, the third right arch (counting from below) may be converted, not into the right subclavian, but into the right carotid, the fourth right arch into the left carotid, and the fourth left arch into the left subclavian, so that we have a supernumerary trunk on the left side, and no provision for the supply of the upper extremity on the right side. It is as though the vascular and the organopoietic layers had been shifted upon one another. Nature provides a remedy by guiding the supernumerary vessel behind the œsophagus and the trachea to the right upper limb, thus placing the *origin of the right subclavian below that of the left one*.

Finally, to this early period of development I must also refer the congenital contraction or *occlusion of the descending aorta*. At the point where the *ligamentum Botalli* is attached to the descending aorta, we find a sharply-defined contraction of the entire tube. In the majority of the hitherto published cases, the lumen of the vessel was entirely obliterated. A collateral circulation had been established between the ascending and the descending aorta by means of anastomoses between the first intercostal, internal mammary, dorsalis scapulæ, subscapular, thoracic and epigastric arteries. It is my belief that this obliteration, which *Rokitanski* particularises as obliteration of the *isthmus aortæ*, occurs before the separation of the heart into a right and a left half—at a time therefore when the blood can still pass through the *ductus arteriosus Botalli* into the descending aorta (fig. 94); for a contraction of the aorta in opposition to the high pressure of the blood would be contrary to all our experience of the mechanics of aneurism.

§ 262. The S-shaped curvature of the cardiac tube advances simultaneously with the partial obliteration of the aortic arches. This it is which determines the position of the heart. For as soon as it is complete, we find the lower loop of the S, the future apex, turned towards the left side, we see the venous sinus entering below and behind from the right side, and the aorta given off above and in front, towards the right, bending back to form the arch with the second turn of the S (fig. 95).

If we inquire into the mutual interconnexion of these phenomena, we shall find it necessary to give an indirect and circuitous answer. We must start from the proposition that a column of fluid, driven through an elastic tube under high pressure, tends to assume a spiral form. This is easily shown by fastening a relatively narrow tube of gutta-percha to the nozzle of a water-tap, from which a full and powerful stream is issuing. Even the simple cylindrical column exhibits the rotation when it is looked at, if possible, in front or from behind; but if we compress the aperture of exit slightly, so as to give it more of an oval form, we may see the spiral curve of the flattened column from the side as well. The experiment is really superfluous, since we perform it every time we pass water. It is only when the *detrusor vesicæ* is too feeble to drive the urine through the urethra under the usual pressure, that the spiral twist of the stream is effaced; hence its absence is justly regarded as a premonitory symptom of paralysis of the bladder. The above remarks apply with equal force to the flow of the blood through the vessels. The column of blood *is* spirally twisted, or, what comes to the same thing, it *behaves* like a cylinder which has been spirally twisted in one direction; and it imparts this twist to the entire vessel whose form it regulates.

FIG. 95.



The heart of the embryo after the completion of its S-shaped flexure. The trunks springing from the arch in their final order. Ductus arteriosus Botalli.

Whether a body is twisted from right to left, or from left to right, may be seen by approximating any two of its points which are not too far apart, and so making it bend at an angle. Suppose by way of illustration we take a pocket-handkerchief, and after folding it lengthwise, twist it forcibly from left to right; then, holding it vertically, let us try and approximate the two ends which we hold—one in each hand; the immediate result is a loop, with its convexity turned to the left. Now the cardiac tube behaves exactly like this handkerchief, when the aortic bulb approaches the *sinus venosus.* The loop turned to the left corresponds to the heart's apex, while the piece below it represents the inferior cava, that above it, the aorta. The cardiac tube therefore bends, not like a smooth cylinder, but like one which has been twisted from left to right. We may therefore assume that in most persons the column of blood is twisted spirally from left to right, and that to this cause is due the usual position of the heart on the left side.

But there are cases in which this rotatory movement takes place in the opposite direction. In these, the curvature of the cardiac tube corresponds to that of a cylinder which has been twisted from right to left; the heart's apex is directed to the right side, and the asymmetrical viscera, whose development is subsequent in point of time to that of the heart, are completely transposed (*situs viscerum inversus*). The liver lies on the left side, the spleen on the right; the cardia is turned to the right, the pylorus to the left; the right lung has two, the left lung three lobes, and so on. We may infer from this, that the asymmetry of the heart is responsible for whatever asymmetry exists throughout the animal organism.

§ 263. A new phase in the development of the heart is brought to a close by the downward displacement of the common pulmonary trunk along the anterior surface of the *bulbus aortæ*, and the simultaneous development of the septum ventriculorum. This process is also liable to be disturbed. For it sometimes happens that the trunk of the pulmonary artery descends along the posterior instead of the anterior surface of the aorta. We thus find *the aorta placed over the right ventricle, the pulmonary artery over the left one*, a malformation which can only consist with life so long as the circulation of Sabatier remains open, and enables the pulmonary function to be dispensed with.

§ 264. Finally, we have yet to consider *congenital stenosis of the right heart*, and particularly of the *conus arteriosus* and the orifice of the pulmonary artery. This is probably a result of endocarditis during fœtal life. We find just the same state of hyperplastic induration, with which we became acquainted in chronic endocarditis. The general effect of the changes in question is a cicatricial stricture of the orifice. White, glistening bands of connective tissue are put on the stretch whenever we try to open out the cut edges of the *conus arteriosus*. The valves usually appear puckered and thrown into folds, as though their base of attachment had been narrowed. Moreover, the development of all the affected parts appears to have been retarded; they are small and dwarfed. The canal is usually constricted to a degree hardly short of absolute closure; the effects of this constriction are highly complex, owing to the fact that it occurs at a period in the development of the heart, when its separation into a right and a left half is not yet complete. Let us suppose in the first place that the right ventricle cannot discharge its contents through the pulmonary arteries; and let us inquire through what channels it *does* discharge them? Through the aorta. The septum ventriculorum is still imperfect; growing upwards from the apex, it has not yet become attached to the base. It is pushed over towards the left ventricle, so that the dilated orifice of the aorta comes to be placed over the right as well as the left ventricle, comes to spring from both ventricles at once. If we consider further, that by obliteration of the pulmonary trunk, the chief mode of access to the pulmonary circulation is cut off, we are led to inquire how the lungs receive their supply of blood? In the first place, they receive less blood than they ought; the blood accumulates in the venous portion of the systemic circulation; this is the chief cause of the incessant dyspnœa from which persons afflicted with this malformation suffer. Moreover the blood which the lungs do not receive through the contracted pulmonary artery, reaches them from the aorta, partly through the *ductus arteriosus Botalli*, which remains pervious, partly through the bronchial arteries, whose anastomoses with the pulmonary circulation undergo marked dilatation in these cases. Meanwhile it is quite clear that all these arrangements, even when they attain their maximum degree of efficiency, can only afford a sorry compensation for the disturbances produced. For just as in the single-chambered heart of fishes, the arterial and venous blood are mingled in the aorta. The lungs receive blood which is only half venous, and are in consequence less capable of removing the carbonic acid of the entire mass of blood. The blood becomes more venous; it is colder and darker than it ought to be. Add to this the accumulation of the blood in the systemic veins, the inevitable consequence of every disturbance in its passage through the heart, but which is especially marked in cases like this. The veins of the extreme parts, of the lips, eyelids, nose, ears, hands and feet, are permanently distended with blood, so that the blue, livid coloration of those parts, *cyanosis*, becomes one of the pathognomonic signs of the condition in question.

III.—MORBID ANATOMY OF SEROUS MEMBRANES.

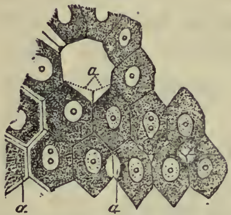
§ 265. A right understanding of the normal condition and the physiological significance of any organ, has always been deemed the most reliable basis for the determination of whatever changes it may undergo in disease. This principle holds good most especially in the case of serous membranes. An error which used to be common in the anatomical description of serous membranes, and one which we occasionally meet with even now, consists in defining them as membranes which differ from the other membranes of the body in possessing a very thin stroma of connective tissue coated with a single layer of pavement-epithelium. This comparison of serous membranes with other membranous structures and particularly with mucous membranes has led the way to many faulty judgments concerning their morbid anatomy. I regard any such comparison as wholly inadmissible.

In order to arrive at a just conception of the real nature and significance of the serous membranes, we must refer to a former disquisition (§ 72), in which an attempt was made to show that the unformed connective tissue of the body was a continuous whole, in which the muscular and nervous fibres, bone and cartilage, epithelial tissues, &c., were embedded. A higher degree of structural union between these formal elements and the associated connective tissue, constitutes "organs," such as the muscles, the membranes, the bones, the brain. Between any two adjacent organs however, there is usually interposed a somewhat thicker layer of connective tissue; and should those organs be obliged in the discharge of their proper functions to glide upon one another, such movement can only become possible if the intermediate layer of connective tissue splits up into two lamellæ, having their opposed surfaces smooth. Now the visceral and parietal lamellæ of any serous sac are just such layers of connective tissue; their membranous character does not denote any organic independence; it is immediately derived from the general continuity of the connective tissue throughout the body. A serous membrane is merely a layer of this connective tissue whose continuity does not happen to be interrupted by the implantation of structural elements of a different order. The serous sac is an interstice—a fissure in the general connective tissue of the organism.

§ 266. This view is hard to grasp; but its value in enabling us to judge rightly concerning all the morbid states of serous membranes can hardly be over-estimated. In the first place, it defines the problem which we have to solve. It implies that the connective tissue of the serous membranes is uninterruptedly continuous with the interstitial connective tissue of those organs which they invest. The inference from this is plain: that the serous membranes may, and do in fact take part in all the morbid changes to which the interstitial connective tissue of those organs is liable. We are compelled for convenience sake to put asunder things which are naturally connected, and to postpone our consideration of a large number of morbid changes in which the serous membranes are involved—viz. chronic inflammations and formative processes—till we come to speak of the several organs. The present chapter will be devoted to those superficial disorders which really are confined to the serous membrane; abnormal secretions, excrescences and parenchymatous alterations—if a serous membrane can be said to have a parenchyma.

§ 267. Let us begin by reviewing briefly the normal anatomy of serous membranes. Here too we shall find our definition of great use, more particularly as regards the epithelium. Everybody knows that the serous membranes are lined by a single layer of pavement-epithelium. Flat, polygonal, nucleated cells form a mosaic; by treatment with silver nitrate their outlines may be readily defined (fig. 96). Is there any tissue in the histological series whose structure seems at first sight to be simpler than that of pavement-epithelium? But this simplicity is only apparent. The question as to the position of the nucleus plunges us at once into difficulties. Is the nucleus lodged in an interstice of the plate, as in the flattened cells of the epidermis? or is the plate furnished with a hole into which the nucleus is fitted like a pane of glass into its frame? Neither of these views is the

Fig. 96.



Serous epithelium (endothelium, *His*). Each cell consisting of a non-nucleated polygonal plate and a nucleated layer of protoplasm. The latter retracted at *a a*. After *Münch*. $\frac{1}{500}$.

true one. The nucleus adheres to one surface, and always to the under surface of the cell.* It is attached by means of a variable amount of finely-granular protoplasm. Thus we see that the cell, apparently so simple, consists of at least two parts; a homogeneous, glassy, polygonal plate, and a nucleated mass of protoplasm. The quantity of the latter is usually just enough to fix the nucleus in its place under the middle of the plate; sometimes, however, there may be enough of it to form a uniform layer, conterminous with the homogeneous plate. In the latter case the cells, when looked at from above, exhibit a finely-granular aspect. On turning our attention, however, to the points at which the individual cells are in contact, we may often observe clear, circular gaps in the granular layer, over which the homogeneous lamellæ extend uninterruptedly. These gaps are due to a slight recession of adjacent masses of protoplasm from one another (fig. 96, *a*).

The simplest explanation of this twofold structure of the epithelial cells is afforded by the conception of the serous cavities as interstices in the connective tissue. The epithelial cells which line the serous membranes are not epithelial cells at all, in the ordinary sense of the word; they do not combine an independent morphological finality with an equally independent functional completeness, like the epithelia of mucous membranes. The epithelial cell of a serous sac is essentially an endothelial element. It originates in a partial hardening of the protoplasm of a soft connective-tissue corpuscle; this portion forming the homogeneous plate, while the residual protoplasm together with the nucleus, remain unaltered. This protoplasmic residue however, belongs at once to the homogeneous plate, and to the intercellular substance of the adjacent connective tissue, it is the vital centre for both. In the peculiar structure of the great omentum we have an opportunity of convincing ourselves of this twofold significance of the serous epithelia. We know that the fully developed omentum is in its finer texture a network, whose trabeculæ are made up of sinuous connective-tissue fibres. It is only the larger trabeculæ which are traversed by an axial blood-vessel. The smaller and smallest ones are simply cylindrical bundles of connective-tissue fibres which contain neither vessels nor cells in their interior. Where then, may we ask, are the corpuscular elements of this connective substance? We must either admit that we have here a connective substance destitute of cells, or we must assume that the nuclei of the superjacent epithelia perform the function of connective-tissue corpuscles as well. The latter is undoubtedly the more correct view. For if we detach the epithelial layer by the aid of dilute acetic acid and a moderate amount of mechanical force, we often find that the nucleated masses of protoplasm remain adherent to the connective tissue, while the plates are set free without their nuclei. The same phenomenon, as we shall see forthwith, occurs at the outset of acute inflammation. Moreover, the products of morbid growth originate from these cells also; so that the pathological histology of the serous membranes is one long chain of evidence in favour of the view that their epithelia are at the same time the outermost cells of the connective tissue.

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* This is unconditionally true only of the adult organism. In the embryo, the homogeneous plate referred to in the text does not yet exist, as a rule; and the future endothelial cells, with their abundant protoplasm, often in a state of active proliferation, lie naked upon the surface of the connective tissue.

As regards the connective-tissue stratum of the serous membranes, I need only say that it is nearly always of extraordinary thinness, and that, particularly in the visceral laminæ of those organs which are subject to considerable variations in bulk, it contains a rich network of fine elastic fibres. These fibres are very welcome to the anatomist as a guide to the extent and limits of the serous membrane in transverse sections.

A. INFLAMMATION.

§ 268. We will concern ourselves first of all with the structural changes to which an inflammatory irritant gives rise on the surface of a serous membrane.*

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* In the following sections I shall often avail myself of the admirable

I can only allude by the way to the great variety of the irritants which determine the course of the inflammatory process in accordance with their respective intensity and quality. Most of them act chemically; the simplest case is when a foreign liquid is extravasated at some point into the serous cavity (perforation of the stomach, intestine or gall-bladder; bursting of an abscess or a gangrenous nodule; entrance of morbid secretions from the uterus and Fallopian tubes into the peritoneal sac, &c.). The etiology of peritonitis, pleurisy and pericarditis in zymotic diseases and rheumatism is more obscure. Here we must recollect that the serous cavities are to be viewed simply as *interstices* in the connective tissue. Hence the fluid contained in the cavities participates in whatever changes the composition of the liquor sanguinis may undergo. Since the discovery by *Von Recklinghausen* of the absorbent stigmata of lymphatic vessels on the serous lining of the diaphragm, we may go so far as to assert that the fluid contained in a serous cavity is subject to a certain change or renewal. Any irritant material which may exist in the liquor sanguinis is thus all the more likely to find its way into the serous cavity. And here, just as in the joints and endocardium, a second factor comes in to increase the irritation (may we say, zymotic?) set up by the *materies morbi;* I refer to the gliding of the opposed surfaces of the serous sac upon one another. In consequence of this, the one surface actually rubs the infecting matter into the other, and I do not scruple to regard this as a concurrent element in the production of the inflammation.

The displacement which the viscera physiologically undergo, and the consequent shifting of the opposed surfaces of the serous sac upon one another, contribute in great measure (as will presently be shown) to the extension of a local inflammatory irritation over the whole of the serous surface.

Owing to their greater simplicity, and the greater ease with which they can be followed, we will first direct our attention to the movements of the lungs in respiration, and the gliding of the pulmonary upon the parietal pleura. During the act of inspiration, the lung expands in all its dimensions; during expiration it undergoes a proportionate contraction. The size and shape of the thoracic cavity adapt themselves at each successive moment to those of the lungs, the contact between them never being broken. How do the pleuræ behave in the meantime? While the pulmonary pleura accompanies the lung in its expansion and contraction, the parietal pleura, attached to the thoracic wall, undergoes the diminution required during the expiratory act, by becoming folded upon itself at its edges. So that it is only at the close of a deep inspiration that the two pleuræ are everywhere in contact (fig. 97). At the beginning of expiration, the edge of the lung (*r*), and with it the extreme

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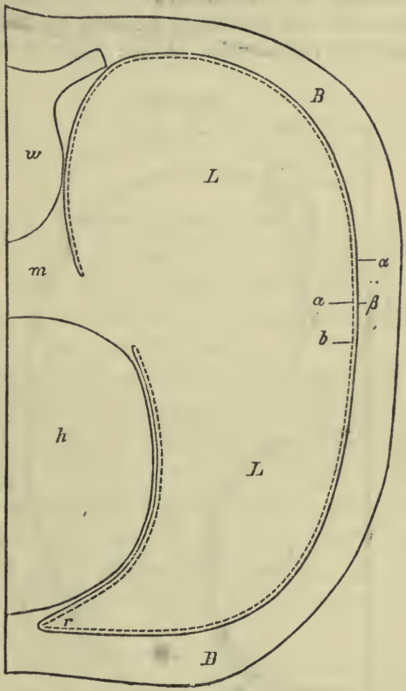
researches conducted in the Pathological Institute of Bonn under my supervision by *Dr. Münch* of Saratof. All the figures marked *Mch.* are borrowed from him.

border of the pulmonary pleura, recede from the anterior fold of the parietal pleura, and glide backwards upon its surfaces, which fall together at the same instant, until a new inspiratory effort separates them (fig. 98). In just the same way, every other point of the surface of the lung is shifted forwards and downwards to a definite extent during inspiration, backwards and upwards to a corresponding extent during expiration; the degree of its displacement being regulated by its distance from the motionless apex on the one hand, and the equally motionless posterior border on the other. Supposing any given point of the pulmonary pleura (*a*) to be wetted by the irritant fluid, it is obvious that this point will advance during inspiration and will contaminate a hitherto unaffected portion of the opposed surface of the parietal pleura (*α*—*β*). During the expiration which follows, a portion of the pulmonary pleura (*a*, *b*) which lies in front of the point originally involved, becomes in-

Fig. 97.

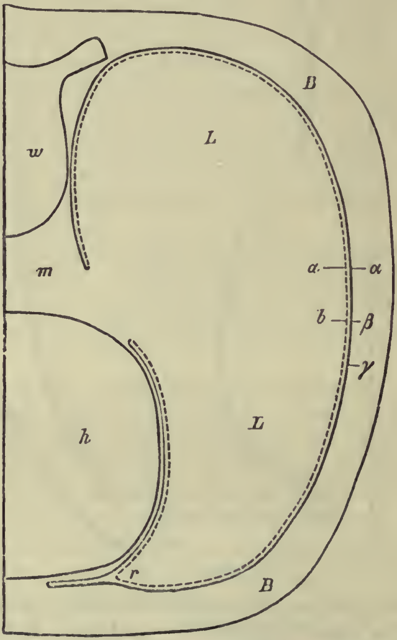


Diagrammatic section through the left half of the thorax, at the end of a deep inspiration. *L.* Lung; *B.* Chest-wall; *h.* Heart; *w.* Vertebræ; *m.* Mediastinum.

fected during the recession of the lung. Lying as this does in front of the primarily affected spot, it will advance beyond this during the next inspiration, and will accordingly contaminate a fresh portion of the healthy parietal pleura (β, γ); in a word, with each breath the patient takes, a new zone, both of the parietal and the pulmonary pleuræ, must become contaminated. The extension of the irritant matter however, occurs with varying rapidity in the various regions of the pleural sac. It hardly amounts to anything in the neighbourhood of the apex and the posterior border, and increases in proportion to its distance from these points, reaching its maximum close to the free borders.

The circumstances are somewhat modified in the case of the peristaltic movements of the bowels. At the moment when a segment of intestine begins to take part in the wave of contraction passing from above downwards along the circular fibres, it forms, in conjunction with the neighbouring segment which is already undergoing dilatation, an inclined plane, surrounding the entire bowel. Upon this plane the general pressure which exists in the abdominal cavity, breaks up into two components; the one, acting at right angles to the axis of the

Fig. 98.



The same at the end of expiration. References as before. For α, β, γ, *see* text.

bowel, tends to compress it, while the other operates along its axis in a direction opposite to that of the contractile wave. This movement is aided by the recoil from the contents of the bowel as they are forced downwards. The former element tends to bring the affected segment into contact with an area of the parietal peritoneum directly proportionate to the length of the mesentery of the affected segment (the attached end of the mesentery acting as a fixed point).

These considerations, into which I cannot enter more at length, since they belong rather to the province of pathological physiology than of morbid anatomy, indicate most clearly, that a perforation of the very mobile small intestine is far more dangerous than one of the fixed appendix vermiformis; that a perforation of the stomach is more serious when it occurs on its anterior aspect and on its greater curvature, than when it is situated on the posterior surface and lesser curvature; that a pleurisy originating at the apex of the lung tends to remain circumscribed, while a pleurisy of the free border rapidly transgresses its original limits, and so on.

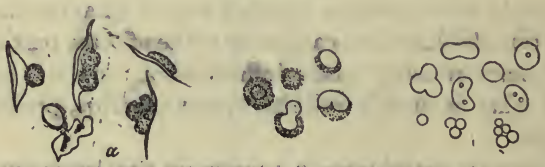
Inflammations of serous membranes are classified on the one hand as acute and chronic, on the other as adhesive, suppurative and indurative. As these varieties shade into one another by infinite gradations, I prefer to adopt a mixed classification of a more immediately practical character.

§ 269.—*Recent inflammation.* The epithelial layer is obviously first exposed to the action of any irritant applied to the surface of the membrane. Hence the earliest phenomena of inflammation will naturally consist of changes in the epithelium. Accordingly these changes, together with a simultaneous transudation from the distended capillaries of the affected part, constitute the first stage of every acute inflammation, and the anatomical basis of what is shortly called a recent pleurisy, pericarditis, or peritonitis.

The serous membrane is reddened; the hyperæmia of the submucous capillaries is apparent even to the naked eye. That the capillaries of the serous membrane itself are gorged with blood and dilated, and that in consequence of this, the intermediate islets of parenchyma seem smaller than usual, may be demonstrated on any detached shred which is examined in iodised serum under a low power. The surface at the same time appears to have lost something of its natural polish; this indicates that the epithelium has become detached, and that the emigration of the colourless blood-corpuscles has already begun. We notice a moderate amount of a reddish, soft and elastic substance which either lies loosely upon some portion of the surface, or stretches in the form of threads and bands between the opposed lamellæ of the serous sac, or else glues them to one another. The last-named phenomenon in particular, prevails wherever two serous surfaces are in contact without gliding far upon each other, as between the adjoining lobes of one lung, between the liver and diaphragm, between the spleen and stomach. Should there be much free fluid present, as generally happens in recent pleurisy, a portion of the "recent inflammatory lymph" is usually suspended in it in the form of ragged flakes. If we take some of this matter, and examine it under a high power, we find large masses of cells and nuclei, together with a lax web of slender fibres, which prove on chemical examination to consist of a coagulated albuminous substance.

a. Fig. 99 represents a large selection of the various forms of cells which were found in the "recent inflammatory lymph," and floating in the exudation, on the first day of a pleurisy excited artificially by the injection of iodine. Among them may be noticed free nuclei with one or more nucleoli, nuclei undergoing division till they are disintegrated into a mass of little spheroids, circular cells with large nuclei and very little protoplasm, some of which are in process of fission; other cells with a large pro-portion of protoplasm, and nuclei already divided. I do not wish to assert that all these structures are derived from the epithelium; the great majority have probably migrated from the vessels in the manner described by *Cohnheim* (§ 89); but I must insist that some, at least, have originated from the epithelium. The tesselated mosaic of cells (fig. 96) has been broken up; the nuclei have lost their usual flattened form and have become globu-

FIG. 99.



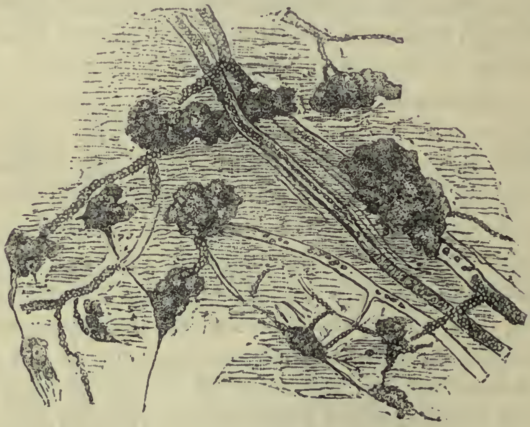
Cells and nuclei from the recent inflammatory lymph. *a.* Their detachment from the homogeneous plates of the serous epithelia. $\frac{1}{500}$. (*Mch.*)

lar; they have also become detached from the homogeneous plates. I cannot, without further reasons, consent to ignore positive results like those figured in fig. 99, *a*. In these cells the nuclei and protoplasm have not yet wholly separated from the homogeneous plates, but the moment of separation is evidently at hand; in one of the cells, the little plate has become quite convex on the side to which the nucleus is attached; in another one, the nucleus is kept in its place only by a fine thread of protoplasm; a third exhibits the simultaneous multiplication of the nuclei by fission. The detached cells continue to undergo proliferation, as we have already seen; in brief, the epithelia which are primarily affected by the irritant, react towards it just as connective-tissue corpuscles would react; the nucleated protoplasm on their under surface producing new masses of nucleated protoplasm by division. The homogeneous plate, deprived of its nucleus, is set free, and may be recognised, even long after, floating about in the serous cavity.

b. The coagulated albuminous substance, which is associated with cells and nuclei in the recent inflammatory lymph, has nothing whatever to do with the epithelium. It is rather to be viewed as an essential constituent of the inflammatory exudation. The high degree of tension to which the blood in the congested vessels of the serous membrane is subjected, naturally causes an exudation of the liquor sanguinis to take place. We may convince ourselves of the great ease with which such a transudation may set in and continue, in any hyperæmia of artificial origin, whether it be active or passive. The exudation resembles the liquor sanguinis in qualitative composition, though its chemical elements are combined in different proportions. The proportion of albumen in particular is very variable, being now above, now below, the standard of the liquor sanguinis. From a histological point of view, we must confine our attention to that element of the exudation of which we have already spoken—the element which passes at once into the solid state—and which is briefly termed "exudation-fibrin." This term implies the assumption that the fibrin of the blood makes its way to the surface of the serous membrane together with the liquor sanguinis, and that, on its arrival there, it is deposited in a solid form. Is this assumption correct? *Virchow* has put forth the view that exudation-fibrin, like fibrin generally, is a product of the activity of the tissues themselves—that it is autochthonous—originating therefore, in the present instance, in the parenchyma of the serous membrane itself. I cannot agree to this. On examining the surface of the inflamed membrane by reflected light, a keen eye may here and there detect little punctiform elevations, closely set—minute buttons of a transparent substance. If the serous membrane is carefully peeled off and examined with a low power (fig. 100) we perceive at the first glance that the position of these nodules is everywhere determined by the course of the vessels. They form rounded masses of an amorphous and homogeneous material which looks as if it had oozed out of the capillaries and arterioles (Uebergangsgefässe) at various points, like rosin from a fir-tree. I regard this appearance as very suggestive. I believe that it enables us to ascertain the immediate source of the exudation-fibrin, which is in fact identical with the fibrin of the blood.

The form exhibited by the coagulated fibrin under the microscope is not always the usual one of a delicate reticulum of felted threads, such as exists in ordinary coagula; the mass is often less fissured, and consists of broad, wavy fibres, differing from areolar connective tissue only in the absence of any regular arrangement of those fibres. On the whole, it is as easy to dis-

Fig. 100.



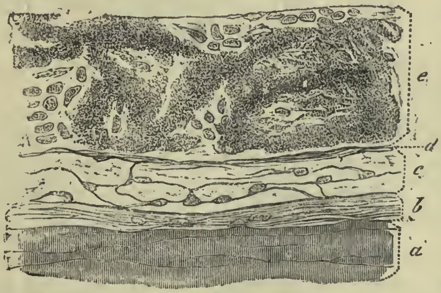
Inflamed peritoneum. Hyperæmia and exudation. (*Mch.*) $\frac{1}{100}$.

tinguish the fibrin by its irregular appearance from every other constituent of the exudation, as it is difficult to convey any idea of the difference in words. It resembles neither a crystal, nor a cell, nor a fibre; it is a coagulum, for the appearance of which I refer the reader to figs. 100 and 101.

§ 270.—*Adhesive inflammation.* The two issues which are common to every inflammatory process, towards organisation on the one hand, towards suppuration on the other (§§ 91-106) recur as usual in the case of serous inflammations. They are doubly interesting in the present case however, inasmuch as they are modified in accordance with the anatomical peculiarities of the tissue, and agree with the typical forms already described only in their essentials. So much must be borne in mind from the outset. We have to do with two opposed surfaces of connective tissue. Now if these surfaces produce the same material, and this material is capable of being organised, the two layers may readily become fused with one another; indeed it would furnish matter for surprise were such fusion not to occur here and there. Indeed it is quite a usual outcome of organisation for the opposed surfaces to become united by bridges of connective tissue over an area of variable extent. Such bridges are called "adhesions," and the epithet "adhesive" is transferred to such inflammations as tend from the first to result in organisation of the inflammatory products.

§ 271. The histological details of adhesive inflammation differ according as the inflamed surfaces of a serous membrane

FIG. 101.



Adhesive inflammation. Diaphragmatic pleura. *a.* Muscular substance of the diaphragm; *b.* Subserous tissue; *c.* Serous membrane; *d.* Boundary-line between the serous membrane and the exudation; *e.* Exudation. $\frac{1}{400}$. (*Mch.*)

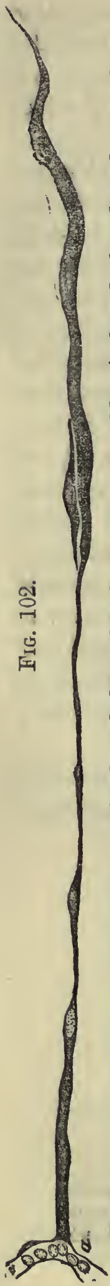


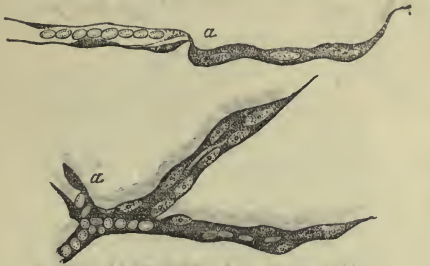
FIG. 102.

Development of vessels in a layer of adhesive lymph from the pleura, five days old. A thread of nucleated protoplasm of enormous length marks out the course of the future capillary; at *a.* the parent-vessel. $\frac{1}{500}$. (*Mch.*)

are or are not separated from the first by a considerable amount of free fluid. In the latter case, the surfaces remaining in absolute contact throughout, the recent lymph suffices as a rule to produce connective tissue, *i.e.* adhesions, from its own resources. This might well be thought paradoxical, so long as this substance was held to consist of fibrin only; such an exudation, destitute of corpuscular elements, must necessarily have been considered incapable of undergoing organisation. We know now that fibrin is only one of the constituents of the inflammatory lymph. It forms a spongy framework (fig. 101) in whose innumerable pores the young cells, multiplied it may be by fission, are contained (fig. 101, *c*). These young cells are not so closely packed as to justify us in giving the name of embryonic tissue to the material which occupies the interstices of the fibrinous network; it may be compared more aptly to mucous tissue, in that a certain quantity of a homogeneous, transparent intercellular substance holds the cells asunder. But there is not a shadow of doubt that this material passes directly into connective tissue, that blood-vessels are developed in its substance, and permeate it—in a word, that it is physiologically equivalent to embryonic tissue. We may observe how the cells which were originally round, become spindle-shaped; how their processes come in contact with each other and are fused together; and how that, no sooner is a greater resemblance, even in outward feature, established between this and the well-known forms of connective tissue (particularly inflammatory spindle-cell tissue, § 93), than the second act in the process of organisation, the development of vessels, sets in. There is no better opportunity than this, of studying the histological course of the secondary and tertiary modes of vascularisation.

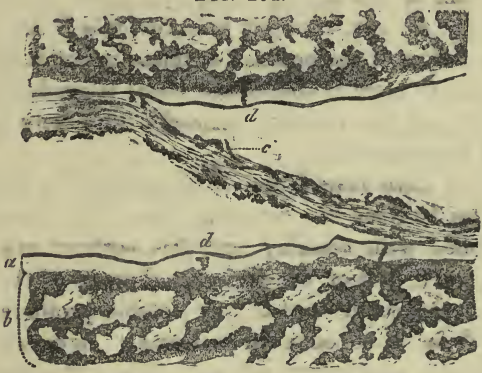
The specimens (figs. 102 and 103) were taken from a false membrane between the adjacent lobes of the right lung in a dog, on the fifth day after a pleurisy had been artificially excited by the injection of iodine. They illustrate in the plainest way the mode in which the vessels are developed; their first appearance as threads of nucleated protoplasm formed by the fusion of cells arranged in rows, the excavation of a channel for the blood, &c., exactly as I described them on a former occasion. Figs. 104 and 105 show that the extension of the vessels occurs

FIG. 103.



Development of vessels and opening of a path for the blood. The course of the vessel is indicated by a cord of cellular masses of protoplasm fused together. Some of the blood-corpuscles have already forced their way into the protoplasm. $\frac{1}{500}$.

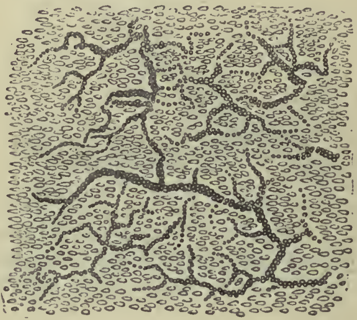
FIG. 104.



False membrane between two pulmonary lobes permeated on either side by a capillary network. *a.* Serous membrane; *b.* Lung; *c.* One of the capillary networks of the false membrane; *d.* A limited number of afferent and efferent trunks. $\frac{1}{100}$. (*Mch.*)

primarily in a horizontal plane. It is only at a few points (at *dd*, in fig. 104) that the afferent and efferent parent-vessels make their way up through the serous layer, while in detached shreds of the membrane, examined from above, a vascular network of exceeding beauty may be observed (fig. 105).

Fig. 105.



Vessels in a false membrane seven days old. $\frac{1}{100}$. (*Mch.*)

In the primary mode of adhesion, that which we are now considering, each of the serous surfaces generates its own vascular network. Thus the transverse section delineated in fig. 104 shows two networks in one and the same false membrane, separated from each other by a layer of tissue which is not yet vascularised. At a later period however, this becomes modified. For if the fusion of the opposed surfaces is not interfered with, the intermediate layer of connective tissue is gradually furnished with vessels, and the vascular networks ultimately unite by innumerable anastomoses.

So far we have traced the development of a layer of connective tissue between the serous surfaces, thin indeed, but very richly supplied with vessels; and this without any active cooperation on the part of the fibrinous element of the exudation, and without the occurrence of any notable proliferation in the subepithelial layer of connective tissue. We can easily lay hold of this false membrane, and strip it from the serous surfaces on which it lies. The ease with which this can be done, spontaneously reminds us of the ease with which the epidermis can occasionally be stripped from the inflamed cutis—and recals the fact, that up to this time the only real connexion between the serous membrane and the false membrane which covers it, is operated by the few and feeble afferent and efferent vessels. At a later period we find the state of things altered. The union between the serous and the false membrane grows more intimate, and finally becomes so close that any attempt to scrape or peel the latter off would be futile; the false membrane assuming the character of an exceedingly intimate and wholly inseparable bond of union between the opposed surfaces. The adhesion is then complete.

§ 272. The phenomena which manifest themselves when the opposed walls of a serous sac are separated from the first by a considerable amount of exuded fluid, and when this separation is kept up for any length of time, are far more complicated. If we consider adhesion, not only as *a* result of, but as *the* mode of repair after inflammation, and in one sense as the goal towards which every superficial inflammatory product tends, and on arriving at which it may be regarded as mature, we must admit that the means for attaining this end which are at the disposal of the serous membranes, are far from being exhausted with "primary" adhesion. They may unite not only by the first or second, but by a third intention also. Of union by the first intention I have already spoken; the second mode is analogous to the repair of wounds by the second intention, to organisation after suppuration, with which we shall deal hereafter.

Union by the third intention is peculiar to serous membranes; it stands between the other two. The surfaces which tend to cohere are held asunder, not by pus or air, but by a fluid, abnormal indeed as regards quantity, but differing in no essential qualitative character from that which is normally present in the interior of a serous cavity. It has no irritating properties; but it hinders union, and gives room for very considerable proliferation on the affected surfaces. The products thus formed have their source, not in the epithelial layer, but in the parenchymatous connective tissue of the serous membrane; looked at broadly, they present, as *Rokitanski* has already shown, the characters of a proliferation of embryonic tissue, of a granulation. But I must not anticipate.

§ 273. We are now entering upon the consideration of by far the commonest variety of pleurisy and pericarditis; it is usually of rheumatic origin, and sets in with an abundant sero-fibrinous effusion. We may suppose a loud, grazing friction-sound to have been heard at first all over the affected region; this became limited to the upper part of the serous sac, while the lower part was filled with fluid. The extent of effusion might have been determined by percussion. The pyrexia was intense, and the patient succumbed when the disease was at its height, partly to the fever, partly to the obstacles in the way of the pulmonary or the cardiac movements. We lay open the pleural sac or the pericardium, and we find it filled to a greater or less extent with a clear, straw-coloured fluid, in which are suspended soft shreds and flakes of a yellowish-white colour. The lining membrane is coated with a pale, yellowish or reddish, transparent or opaque, coherent and elastic, or brittle and friable substance, from which it is distinguished partly by its colour and consistency, partly by the fact that this matter can be stripped or peeled off with varying degrees of facility. The aspect and general arrangement of this substance gives us the notion of a soft, plastic material having been introduced between the layers of the serous sac and subsequently moulded by the movements of the lungs or heart as the case may be. A portion of it has accumulated at those points where it is least in the way of the movements of the viscera; it occupies all the chinks and corners, it fills up the inflexion of the pleural sac between the diaphragm and the thoracic walls, it obliterates the cardiac sulcus and the fold of pericardium which is reflected over the great vessels. But where the substance in question forms a thick layer on the surface of the heart or lungs, it exhibits a peculiar reticulated or villous aspect, such as might *a priori* be expected from a consideration of the alternate apposition and separation of the visceral and parietal lamellæ; these appearances may be exactly imitated by squeezing a layer of putty between two plates of glass, and then tearing them apart.

The *ensemble* of these characters indicates a close analogy with coagulated fibrin; and there has long been a tendency to regard this material simply as fibrin exuded from the blood, and to assume that it subsequently formed the adhesions. Various protests against this assumption were however lodged at an early period. *Reinhardt* in particular denied the possibility of pure fibrin ever becoming organised, and was the first to describe how it underwent transformation into a fatty-mucous, opaque material, which ended in becoming dissolved or caseous, and never in being developed into connective tissue. Notwithstanding his arguments, this misconception held its ground, until *Rokitanski's* teaching, to which allusion has been already made, paved the way for our present doctrines as developed by *Buhl.*

In accordance with their researches, we must divide the layer of exudation, which lies loosely on the serous surface, into two strata: 1. An upper one which, during the height of the inflammatory process, assumes a disproportionate thickness; this layer really does consist of fibrin, and covers in the subjacent one at every point. The fibrin accumulates in greatest amount on those parts of the affected organ which undergo most displacement, as *e.g.* on the free borders of the lungs; just as in whipping the blood to free it from its fibrin, the latter coagulates in flakes upon the stirring-rod. The appearance of the exuded fibrin under the microscope has already been described (§ 269). It forms the same coarse network as in primary adhesion (§ 271); it differs however in not being of the same thickness throughout, varying in this respect from a quarter of a line to six lines or more. 2. A deeper stratum of young connective tissue formed by a proliferation of the connective tissue of the serous membrane. We may assume that as soon as the serous surface is denuded of its epithelium, the inflammatory action extends into the connective-tissue layer of the serous membrane; but without attaining any considerable intensity till from the third to the seventh day of the disease. On examining sections, we find a number of connective-tissue corpuscles in the parenchyma of the serous membrane; their numbers increase as we approach the surface on which they are set free. Upon this surface they appear embedded in a clear matrix, containing mucin, together with which they make up the layer of embryonic tissue which we are now considering. Both cells and matrix must be viewed as a true efflorescence from the serous membrane; the true "plastic exudation" is really formed by them, and not, as used erroneously to be supposed, by the fibrin.

§ 274. As regards the external form of this recent "connective-tissue efflorescence," we need only remark that for obvious reasons, it cannot arrive at any independent finality. Judging from the analogy of recent layers of embryonic tissue occurring elsewhere, we may indeed infer that it *tends* to assume the form of a membrane roughened by villosities. But this tendency is counteracted on the one hand by the repeated mechanical disturbances to which it is exposed, while on the other it is rendered impossible at most points by the superimposed layer of fibrin. Hence the granulation-tissue forces its way up into all the interstices of the fibrinous stratum, grows round it and through it layer by layer, and thus attains a considerable degree of thickness earlier than it would otherwise have been able to do. Notwithstanding even this intimate penetration, in which the fibrin acts the part of a supporting framework, we must reject any claims to an active share in the organising process, which may be urged on its behalf.

Close upon the heels of this development of embryonic tissue comes vascularisation. An extraordinarily rich network of capillaries speedily permeates the young false membrane. The newly-formed vessels are characterised by their exceptionally wide calibre, and as is often the case with young vessels, by the thinness of their walls. On the other hand, the afferent and efferent vessels of the serous membrane are few and narrow. The result is an arrangement resembling that of the *retia mirabilia*, where the blood-pressure is proportionately heightened by the intervention of a capacious channel between an afferent and an efferent vessel. A like result may be anticipated in the present instance; —and that the blood in the newly-formed capillaries is really under a far higher pressure than in those of the serous membrane, is proved by the number of extravasations which ensue both in the interior, and upon the surface of the false membrane, giving it a reddish and mottled colour; while the free fluid is likewise tinged with red. Accordingly, the vascularisation of the false membrane leads in the first place to a state of things most critical as regards the general course of the disease—a state of things which not only affords the most favourable conditions for the continuance of the exudative process, but also, by supplying an abundance of nutrient matter, favours to the utmost the formative changes in the false membrane itself. At this point therefore, the patient is threatened with an over-production of cells—with suppuration. The practitioner detects the unfavourable turn the disease is taking, and expresses his fears by saying that it drags, that absorption has come to a dead-lock, &c.

§ 275. But we must defer considering the dangers of suppuration for the present. Let us first of all take the course of the inflammatory process when it remains true to its original, adhesive character. We may justly inquire how, under the conditions described above, the process of exudation can ever come to a stop. Now one reason for its cessation lies in the conversion of the young embryonic tissue into fibrous connective tissue. This transformation, as was fully shown in § 93, is invariably associated with a certain amount of contraction which, in its turn, leads to the obliteration of a great majority of the newly-formed vessels, so that the blood-supply of the fully-developed adhesions represents but a very small fraction of the original capillary network. On the other hand, we must remember that although the fibrin, which is not merely applied to the surface of the young connective tissue, but sends countless processes into its substance, does not undergo organisation, it nevertheless shrinks uniformly and with great force. This shrinking sets in directly after its coagulation, and progresses steadily when the conditions are favourable (and where could it find conditions more favourable than the present?), until it has attained the smallest volume of which it is capable, or until some other sort of metamorphosis has robbed it of its most characteristic property. It is obvious that this contraction of the fibrin must affect the granulation-tissue with its vessels, which it covers and includes, and so must check the further progress of the transudation. Be this as it may, transudation is arrested, and absorption takes its place. The shreds and flakes of fibrin which are freely suspended in the exudation begin to undergo mucous and fatty degeneration;—the soft, swollen material is found to contain innumerable oil-globules, which may however originate in a fatty transformation of its contained cells. This degenerating fibrin presents a whitish and opaque aspect to the naked eye; if the effusion happen to be absorbed with exceptional rapidity, a portion of fibrin may remain undissolved, and dry up in some corner of the serous sac, where it becomes cheesy and remains for years in this condition. As a rule indeed, both the suspended fibrinous flocculi, and the fibrin which coats the connective-tissue efflorescence on the walls of the cavity, undergo complete solution in the effused fluid before it disappears, and are subsequently absorbed into the blood together with it. The opposed serous surfaces are approximated until they touch each other, when the inflammatory products by which they are coated, coalesce. Soon too, the bridge along which the vessels of the parietal and visceral laminæ anastomose with one another, is completed.

This series of changes finally results in the formation of those well-known "bands of adhesion," which connect the costal with the pulmonary pleura, the heart with the pericardium, the various abdominal viscera with one another, and with the abdominal wall. Their minute structure has often been investigated; like the serous membranes, they are coated with a single layer of pavement epithelium; in addition to this, they contain wavy bands of connective tissue, between which run long and slender blood-vessels; newly-formed nerve-fibres have also been found on one occasion in an adhesion (*Virchow*). What seems to me most important is the fact that in the present case, the continual shifting of the opposed surfaces on one another, the incessantly renewed approximation and separation of the two ends of the adhesion, exert a modifying influence upon the organisation of the embryonic tissue; the resulting connective tissue, instead of assuming the character of ordinary cicatricial tissue with its short, inelastic and rigid fibres, approaching more nearly to the normal type of lax areolar tissue.

Thus it is clear that the final result of the inflammatory organisation depends very materially on the external conditions under which it takes place; and that in particular, a repeated stretching and relaxation of the cicatrix determines the production of a true lax areolar tissue in place of the inelastic cicatricial tissue.

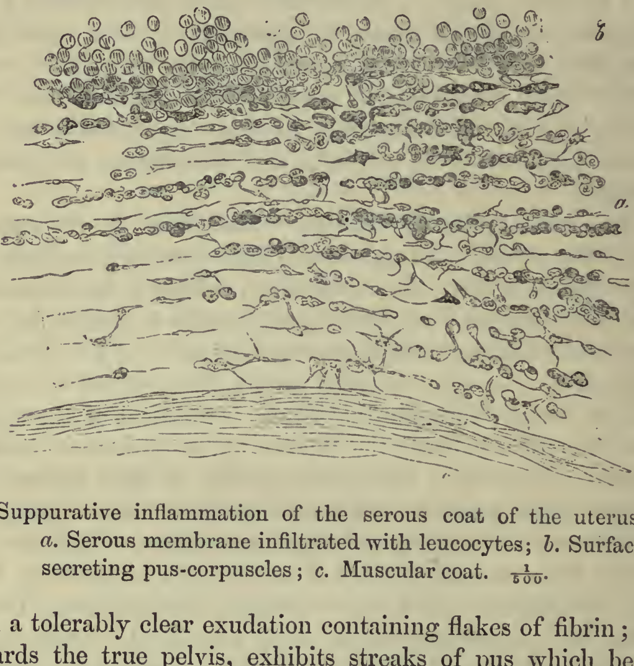
§ 276.—*Suppurative inflammation.* We distinguish two varieties of suppuration, primary and secondary. Most abdominal inflammations, particularly those which are caused by perforation of the alimentary canal, or by infection from the organs concerned in parturition (puerperal fever), afford abundant opportunities for the study of the former variety. If the inflammation happen to be quite recent (as in the so-called *peritonitis fulminans*) we may easily convince ourselves that in this, as in the adhesive variety, a stage of "recent agglutination" opens the series of morbid changes. In fact, the histological transformation of the fresh adhesive matter into pus, appears to take place as readily as that into connective tissue. The neutral cells which are present are pus-corpuscles from the moment when they are suspended in a serous fluid and proceed to divide and multiply therein.

Their development into "specific pus-corpuscles," *i.e.* into young cells with several nuclei, is in no respect essential; though it may nevertheless be frequently observed. The transition presents itself to the naked eye as a yellowish-white discoloration and liquefaction of the reddish membranes and shreds, beginning at their edges, and terminating in their rather sudden dissolution into a puriform fluid. I have succeeded in demonstrating this more than once in peritoneal inflammations excited artificially; at the same time however, I noticed that the stage of "recent agglutination" in primarily suppurative inflammations was generally of very brief duration, passing very speedily into the essential phenomenon of suppurative inflammation, *sc.* purulent exudation.

The case is primarily one of "exudation" in the strictest sense of the word. Vast numbers of leucocytes migrate from the dilated blood-vessels; they first of all infiltrate the connective tissue, and then—as I am forced provisionally to assume in order to account for the occasionally enormous quantity of pus—undergo proliferation. As may be seen in fig. 106, which represents a vertical section through the serous investment of the uterus, all the interstices between the thicker fibrous strata are literally crammed with cells. The great variety of flask-shaped and analogous forms indicates moreover that these cells are not quiescent, but are undergoing amœboid movements. The direction in which these movements tend is hardly open to question; it is clearly upwards and outwards. One may figure to oneself how, through the membrane which is so abundantly infiltrated, a mighty stream of exuded liquor sanguinis is passing. This also will tend to make its way through the interstices between the fibres, and will consequently carry with it numbers of the corpuscular elements which they contain; these cells it will afterwards hold in suspension as pus-corpuscles, when it comes to rest in the serous cavity. In this manner does the exudation become purulent on its way from the blood-vessels to the free surface of the serous membrane; this is the rationale of purulent exudation.

At an early period, while the corpuscular secretion is still moderate in amount, the exudation is clear and deposits an abundance of transparent, gelatinous flakes of fibrin; at a later stage, it consists of pure, greenish-yellow, thin pus. In examining the bodies of patients who have succumbed to puerperal peritonitis we often find the recent inflammatory agglutination in the upper regions of the abdomen, in the neighbourhood of the stomach and liver; lower down, about the kidneys and between the mesenteric folds of the upper coils of the small intestine, we meet with a tolerably clear exudation containing flakes of fibrin; this, towards the true pelvis, exhibits streaks of pus which become more and more numerous, till, in the pelvic cavity itself, the fluid becomes entirely purulent. To the naked eye the serous membrane appears hyperæmic; but the red hue of the injected vessels is toned down by a milky cloudiness which covers it as with a veil. This is due to the purulent infiltration of the membrane itself.

FIG. 106.



Suppurative inflammation of the serous coat of the uterus. *a.* Serous membrane infiltrated with leucocytes; *b.* Surface secreting pus-corpuscles; *c.* Muscular coat. $\frac{1}{500}$.

§ 277. Side by side with the primary form of suppurative inflammation, we may study those cases in which a process, primarily adhesive, passes into the suppurative form. It has been already shown that this transition is favoured and ushered in (anatomically speaking) by the luxuriant vascularisation of the young false membranes, which furnishes materials for a more exuberant corpuscular proliferation, *i.e.* for suppuration, when the inflamed membrane is exposed to any fresh source of irritation. The practitioner is usually warned of the unfavourable turn which the disease is taking, by the occurrence of a severe rigor and the hectic fever which follows it. Quite suddenly, as it seems, the cell-proliferation enters upon a more active phase. Every variety of cell, whether it be situated in the exudation, in the false membrane, or in the serous membrane itself, takes part in the process. The clear serum becomes turbid. Whole shreds of the false membrane are loosened from their connexion with the underlying tissues and detached, preliminary to their liquefaction into pus; denuded patches of the serous membrane itself undergo losses of substance, which however, are always shallow. Such ulcerations are not uncommon on the costal pleura where it lines the ribs; they extend into the subserous connective tissue, and more rarely to the periosteum and bone, which is consequently laid bare and undergoes necrosis. Apart however from such accidents, the suppuration retains its superficial character even in its most acute forms. The suppurating surface of the serous membrane is analogous, not to a destructive ulcer, but to a productive and granulating wound. The analogy with a superficial wound holds good moreover as regards its limitation on the side of the serous cavity by a membrane of young connective tissue studded with granulations—the "pyogenic membrane" of authors. The healing process begins in exactly the same way, when the inflammation has been of the purulent order from the first.

In the meantime, an accumulation of pus, often colossal in amount, has been forming in the serous sac. This is not surprising when we consider how large a quantity of pus may be secreted even by comparatively small ulcers; and in the present case we have an ulcerating surface which is measured not by square lines, but by square feet. It is common enough to see half a pailful of pus removed from an empyema by tapping during life or after death. The diaphragm is pushed down together with the liver or the spleen, the intercostal grooves are effaced, the lung undergoes a diminution in size greater than could be produced by its own elasticity; it contains no air, and hangs in the purulent fluid as a narrow strip of leathery tissue, hardly as broad as the hand. Finally, the pus seeks a mode of exit, just like an abscess. In the case of an empyema the spot chosen for perforation is usually one of the lower intercostal spaces; here however the art of the physician usually interferes, disturbs the natural but somewhat tardy course of events, and determines the point of exit with a trocar.

§ 278. As regards the further progress, *i.e.* the gradual repair of the morbid state, we may argue from our experience of union by the second intention, with this limitation, however, that in the present case cicatrisation occurs on a scale proportionate to the colossal size of the ulcerating surface. We find the usual series of embryonic tissue, spindle-cell tissue, and rigid, short-fibred cicatricial tissue—each member of the series being developed from its predecessor, as is fully set forth in § 93 *et seqq.* The cicatricial tissue presents itself in no small proportions; it forms a white and lustrous, fibroid stratum, from half a line to three lines in thickness, which clothes the serous cavity, and is stretched over the adjacent organs. This huge cicatrix contracts like any other scar, and causes mechanical effects of an imposing order. It is an admirable illustration of the gigantic results which nature is able to produce by the additive repetition of fractional moments of the same order. And yet the resistance to be overcome during the healing of an empyema which has opened externally, is nothing less than that of the vaulted arches of the thoracic skeleton which have to be dragged inwards, in a direction, that is, which the whole aim of their being is to resist. There is an erroneous impression afloat, that the cicatrising process is able to help the expansion of the collapsed lung. But experience teaches us, as might have been expected *a priori*, that it is the fibroid tissue which serves permanently to compress the lung. Sooner than allow of any such expansion, the remaining thoracic viscera, *sc.* the heart, are dragged over to occupy the space which was formerly filled by the collapsed lung. No Torricellian vacuum is produced. The stress is borne by the neighbouring organs, which are dragged out of their places. The fibroid sac into which the pleura has been converted must and will contract just as a urinary bladder contracts. And this contraction occurs with such force that not only are the soft and yielding thoracic organs compelled to follow it, but the ribs also are dragged downwards and inwards till they overlap one another like the tiles on a roof; the vertebral column itself undergoing a corresponding curvature. At the same time, the size of the cavity is proportionately lessened; a few drops only of pus occasionally dribble from the fistulous orifice. And the process of repair is brought to a close by the total obliteration of the cavity.

B. NON-INFLAMMATORY FORMATIONS.

§ 279. Were I in this place to consider all the cancerous, sarcomatous, chondromatous and lipomatous affections which are occasionally met with in serous membranes, I should be obliged, not only to recapitulate what has already been laid down concerning morbid growths in general, but to anticipate in great measure the diseases of the alimentary canal, the lungs, liver, &c. For the serous coat of any organ stands simply in the relation of adjacent connective tissue towards those heteroplastic growths which have their origin and seat in the parenchyma of the organ itself; and it is in this capacity that it shares in the neoplastic process. The present chapter will therefore be restricted to the consideration of such growths as originate primarily in the serous membranes and run their course mainly within their parenchyma.

§ 280. Foremost among these stands that overgrowth of connective tissue which occurs in the walls of a serous sac during the continuance of a chronic dropsical effusion. The first stage of the process presents itself to our eyes as a milky cloudiness of the membrane. This is partly due to a moderate degree of thickening, but mainly to an alteration in the consistency of its fibres. *Virchow* has given the name of "sclerosis" to that condition of the fibres of connective tissue, in which their bulk is but little altered, while their solid contents (*i.e.* their density) are considerably increased. Such fibres are stiffer than usual; they are less capable of swelling by imbibition; they are, upon the whole, more indifferent to reagents, and refract light more highly. It is this latter property which gives the sclerotic patches of the serous membrane their milky opacity. The essential nature of sclerosis is quite as obscure as that of the processes with which it is associated. As regards these, we do not know whether the transudation is simple or inflammatory; as regards the sclerosis, whether the hyperplastic change belongs to one or other category. In my opinion we must draw as marked a line as we can between active and passive congestion; hence we must seek the origin of the disease either in an inflammation, or in a passive disturbance of the circulation. In the majority of cases, our search will be successful. We cannot but admit, however, that passive congestion is a powerful predisposing cause of inflammation; also, that in every inflammatory hyperæmia a statical element is evolved from the unquestionable dilatation of some portion of the circulatory tract. Accordingly, both sets of phenomena are often intimately associated with one another, and are often so blended that it becomes a matter of the greatest difficulty to determine how much is due to the one, and how much to the other element. Instinctive tact and practical experience are here our best allies. We usually regard the hydrothorax of valvular disease as a passive transudation, while we take the dropsy of the tunica vaginalis propria testis (hydrocele) to be the type of an inflammatory dropsy. Between these extremes we have dropsy of the pericardium and peritoneum, and dropsy of the ventricles of the brain; the former more nearly related to hydrothorax, the latter to hydrocele. Effusions into bursæ mucosæ, the synovial sheaths of tendons, and the joints, are a debateable ground. The element of uncertainty, the discretionary element, in this doctrine is due to the absence of available criteria for the determination of the exact point at which the transudation on the one hand, and the morbid growth on the other, should begin to be called inflammatory. *Julius Vogel* attempted to establish a criterion for the inflammatory nature of the transudation in the presence of spontaneously coagulable albuminous substances (*Hydrops fibrinosus = inflammatorius*). But now we know that the fluid which accumulates in the pericardium during the death-struggle, and which certainly is not inflammatory, contains fibrinogen. As regards the morbid product with which we are immediately concerned, an attempt has been made to erect it into an inflammatory formation *par excellence;* a proceeding which seems to owe the favour with which it has been received, only to the summary way in which it removes all scruples concerning the *quæstio vexata* of a definite boundary-line between hypertrophy and inflammation. To my mind, there really is no sharp line of demarcation between the two. Inflammation is but a perverted image of normal nutrition, and hypertrophy is but a minor degree of the very same perversion. Of course I do not presume to arrest all discussion by any dogmatic statement; on the contrary, I willingly admit that I do not feel myself in any way ripe for a conclusive utterance on this subject. I seek only to justify myself for describing the changes with which we are now concerned, as simply hyperplastic, without attempting to prejudge their mode of origin and causation from the form which they assume.

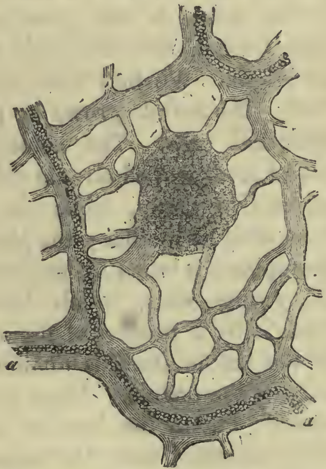
§ 281. The "milky cloudiness" alluded to above, is peculiarly striking when it affects the serous coat of a dark-coloured organ, especially the capsule of the liver or the spleen, and the visceral pericardium (tendinous spots of the heart). Were the brain not itself of a white colour, the sclerosis of the ependyma in chronic hydrocephalus would undoubtedly present itself to our eyes as a milky cloudiness. Sclerosis (to repeat what has already been said) is merely the lowest degree of hyperplastic overgrowth of connective tissue, as regards which it is still uncertain, whether we ought to consider it as a proliferative change, or as a simple condensation of pre-existing connective tissue.

Besides sclerosis, we are acquainted with a whole series of connective-tissue proliferations, which have one feature in common, viz. that they all tend to assume more of a circumscribed character. In closest relationship to sclerosis, we have the development of sharply-defined, flat elevations of *cartilaginous* texture. These are most common on the capsule of the spleen, where they exhibit angular outlines and a yellowish-white translucency, and may attain a height of from half a line to one line. On the pleura they are more circular and transparent, with a lenticular surface; while on the tunica vaginalis of the testicle they are characterised by their often considerable size and hardness. These cartilaginous elevations are closely related to the cartilage of the cornea in their minute structure. Next to them stand *fibromatous* outgrowths. These are especially prone to become polypoid. In the dropsical tunica vaginalis testis, and in the peritoneal cavity, we occasionally meet with free fibrous bodies, varying in size from a cherry-stone to a hazel-nut, of a spherical or spheroidal shape and concentrically laminated structure; these are simply the detached heads of such polypoid excrescences from the walls of the cavity. The softer *dendritic vegetations*, which are less frequent on serous than on synovial membranes, are described by *Rokitanski* as follows:—"Their first appearance is in the form of club-shaped hyaline vesicles (minute granulations of embryonic tissue, *Rindfleisch*); these grow into an arborescent structure, and produce connective tissue in their interior. The clavate extremities of the twigs and branches commonly become flattened into lenticular or melon-seed-shaped bodies, and sometimes exhibit a facetted surface. The primitive nodule often grows into a sacciform cyst, filled with serum, or with a fibrous network whose interstices contain fluid." We may call the latter form a pendulous myxoma. It constitutes a transition stage to the complete liquefaction of the contents of the nodule, which then becomes a pedunculated "cyst due to softening" (Erweichungscyste). The latter are most frequently met with on the peritoneum, and especially on that part of it which clothes the female generative organs—the broad ligaments, ovaries, and Fallopian tubes.

§ 282. The *lipoma arborescens* of *Müller* is peculiar to serous and synovial membranes. I have already pointed out in detail (§ 133) the close analogy which subsists between the central growth of lipomatous tumours, and the dendritic type of structure. We might fairly regard the *Lipoma arborescens* as a *lipoma tuberosum*, broken up into its component elements; but it is better to regard it simply as a hyperplastic development of the familiar villous and polypoid fatty appendages of the serous and synovial membranes (*app. epiploicæ, glandulæ Haversianæ, &c.*).

§ 283. As regards the heteroplastic formations (cancer, tubercle, sarcoma) which occur either primarily or secondarily on serous membranes, there is only one question which interests us as histologists—that concerning the origin of the embryonic tissue, which as we know, forms the common basis of them all. These growths (when they really spring from the serous surface, and have not been propagated *per contiguum* from neighbouring organs) are all strikingly characterised by their very superficial position. Scirrhus looks like a pasty mass "which has been uniformly spread out over the serous surface" (*Rokitanski*); medullary cancer resembles scirrhus, or takes the form of roundish flattened protuberances; colloid cancer occurs "in the form of nodules, which occasionally grow to an amazing size, and are almost free in the serous cavity, *i.e.* adhere to its walls by a few insignificant vascular attachments"; the spindle-cell sarcoma as a fungoid vegetation. Finally, the miliary tubercle looks very like a grey, miliary vesicle. Most of these growths can readily be scraped from the serous surface with a knife; the latter is left somewhat rough, but without any important loss of substance. It is quite clear that the quantity of connective tissue which has been requisitioned from the healthy serous membrane by the growth, is extremely small; hence it is on serous membranes that we are best able to study the essential texture of these growths, with least risk of being misled by adventitious constituents. To what is this superficial localisation due? It is due to the fact that these tumours, taken in the aggregate, are—at least primarily—outgrowths from

FIG. 107.



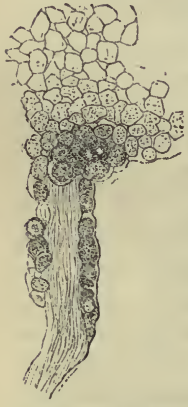
Miliary tubercle of the omentum. $\frac{1}{100}$. (*Mch.*)

the *epithelial layer* of the serous membranes. Nothing hinders them indeed from spreading afterwards, not only into the parenchyma of the serous membrane, but also *through* the parenchyma into neighbouring organs. Wherever connective tissue exists, a path is open to them. We must not forget however, that the epithelia of serous membranes are themselves connective-tissue corpuscles.

§ 284. One example will suffice to illustrate this highly peculiar mode of origin. I choose a miliary tubercle on the omentum. Fig. 107 represents a very small nodule (under a low power), which has not yet grown out of the limits of its birthplace. It consists of a globular aggregate of cells, suspended from nine slender threads of connective tissue radiating from its periphery to the stouter and partly vascular trabeculæ which form the boundaries of one of the larger meshes of the omentum.

Let us examine one of the nine points at which the connective-tissue fibres join the nodule, under a higher power, (×800). Here, at the edge of the formation, we may expect, if the nodule is still growing, to find appearances which will shed light upon the details of its origin. We find what is represented in fig. 108. The nodule grows by proliferation of the epithelial cells. The homogeneous lamella is raised from its bed on one side of the thread of connective tissue, while on the other, it has been shed altogether; the place of the nucleated protoplasm is taken by larger and smaller groups of young cells, which have clearly sprung from it by a process of fission. The substance of the thread itself is unaltered up to the very edge of the nodule. Here it escapes our observation; but in the interior of the nodule it is still connected with the other eight threads in precisely the same way as it was before the growth of the tubercle. It obviously takes no part in the proliferation; and up to this point we are entitled to regard the whole of the new growth as a product of the serous epithelia. Should the centrifugal growth, at a later stage of its progress,

Fig. 108.



Origin of a miliary tubercle by proliferation of the serous epithelia. $\frac{1}{800}$. (*Mch*).

reach the thicker trabeculæ (fig. 107, *a*) of connective tissue, then indeed non-epithelial connective-tissue corpuscles will contribute their mite to the additive enlargement of the nodule. But the size to which the nodule must needs attain before this can possibly occur, proves what the resources of epithelial growth can do without any extraneous help.

IV.—MORBID ANATOMY OF THE SKIN.

§ 285. In studying the structural alterations associated with the various disorders to which the skin is liable, it is of advantage to consider that organ as made up of the epidermis and papillary body on the one hand, of the corium and subcutaneous areolar tissue on the other; the morbid anatomy of the cutaneous glands and the hair being considered by itself in an Appendix.* The papillary body, apart from its other physiological functions, is the matrix of the epidermis. The two structures constitute a vegetative whole; and their continuity is strikingly apparent when, as in the case of most diseases, the vegetative relations of the parts are disturbed. So too the glands, the hair and the nails are all liable to special diseases of their own. Of course I neither care, nor do I wish to deny that the disorders of the various constituents of the integument pass into one another by manifold transitions, that they may coexist, that they may be pathologically identical. No classification of natural objects can lay claim to be absolute; we must endeavour to select that which fits the actual facts most closely. Thus for instance, a similar analysis of the structural constituents of mucous membranes would be far from conducing to a better knowledge of their pathology.

1. DISEASES OF THE EPIDERMIS AND THE PAPILLARY BODY.

a. *Inflammation.*

§ 286. The integument of the body is peculiarly exposed by its position to all external influences of a hostile nature. We are not therefore surprised to find a long series of skin-diseases caused by external irritants. And here we must not confine our thoughts to single impressions of a violent kind, such as blows and knocks, but include likewise those more chronic or recurrent irritations of the surface, trifling in themselves, which are caused by dirt, vermin, scratching, exposure to the weather, improper clothing, and the operation of chemical and mechanical irritants.

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* The nails will be dealt with among the horny overgrowths of the epidermis, the keratoses.

These trivial sources of irritation are nevertheless powerful enough to affect the specially sensitive papillary body, richly supplied as it is with vessels and nerves, through its cuticular covering. The papillary body reacts to the stimulus by hyperæmia and inflammation; its disordered state is shared by the epidermis, and we thus obtain a group of changes, which are confined, at least in their beginnings, to the papillary body and the cuticle.

There is yet another cause to be considered. We know that in infectious diseases, when the general malady has reached a certain height, some individual organ is usually specifically involved. We express the fact by saying that the disease becomes localised, and with this phrase we connect some vague idea of an elimination of the *materies morbi.* It is true that these foci of disease are very commonly situated in secretory organs. In small-pox, measles, and scarlet fever, the skin is the selected organ; it is supposed moreover that nettlerash, erysipelas, some forms of herpes, and a large proportion of chronic dermatoses, depend on the localisation of some constitutional disease. Now what occurs in every one of these cases is not a mere abnormality of the secretion, as might be inferred from the humoralistic idea alluded to above, but hyperæmia and inflammation; moreover, at least primarily, it is not the whole skin but only its most superficial layers which are involved. The papillary body, strange to say, is the chief seat of the disorder, even when the skin-lesion has been excited by causes operating from within, through the blood. Should this, like our former category, be ascribed to the greater sensitiveness of the papillary body? By no means. We must look elsewhere for the causes of this localisation; and for my own part I cannot help ascribing a peculiar influence in the matter to the distribution of the vessels.

Normal histology has explained the way in which the vessels are distributed in the papillary body (fig. 109). Each papilla is furnished with its own afferent and efferent capillary vessel; the two communicate either directly, by a simple loop, or—more commonly—by a number of loops. These vessels are all remarkably tortuous; it sometimes happens that the afferent and efferent trunks of a simple capillary loop are twisted round each other corkscrew-fashion till they unite at the apex of the papilla. The point at which they unite—the summit of the curve—is always much dilated. Everything points to the conclusion that in the cutaneous papillæ the lateral pressure of the blood must be augmented and the current of the circulation retarded. Indeed we may look upon the vascular apparatus of the larger papillæ, which are provided with several communicating loops, in the light of small *retia mirabilia.** They stand towards the vascular network of the cutis in the relation of diverticula; like the side-channels of a stream, in which the current experiences greater resistance, notwithstanding that the fall is the same in either case. This arrangement may have a physiological importance of its own, it may be of the utmost moment for the respiratory function of the skin; apart from this however, it serves to explain how it is that hyperæmic conditions of the skin, to whatever cause they may be due, are peculiarly intense and lasting, and lead to more serious consequences in the papillary body than elsewhere.

What is true of the papillary body as a whole is peculiarly true of the smaller, but all the more thickly-set papillæ which surround the orifices of the hair-follicles (fig. 109). Here too therefore, in connexion with hyperæmic conditions of the entire tegumentary system, the dilatation of the capillaries, the slowing of the blood-current, and all the derived phenomena, attain their maximum intensity. In a word, the vascular apparatus of the subepithelial connective tissue of the skin is disposed in such a way as to bring the limitation of so large a number of derma-

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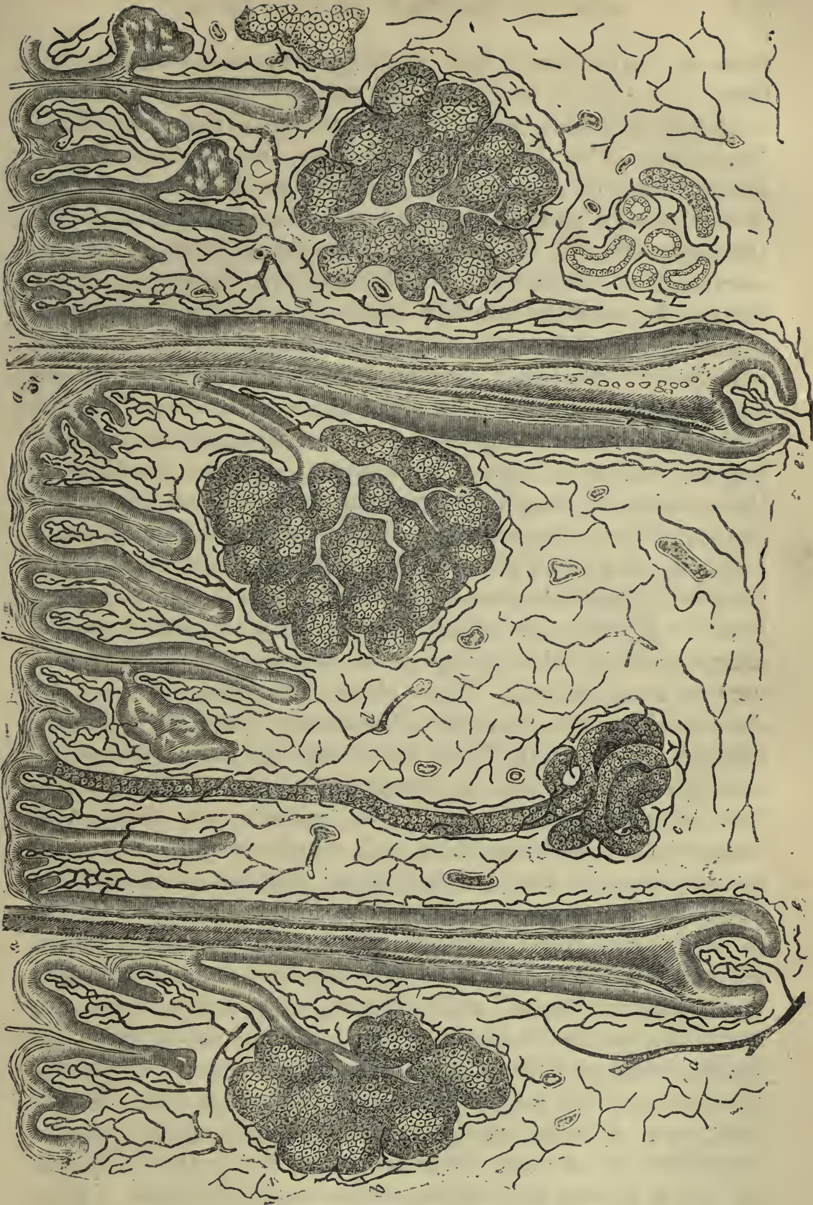
* In injected specimens of the kidney, I have often observed that the Malpighian glomeruli are also made up of two or three capillary tufts (Gefässbäumchen), each of which corresponds precisely to the capillary tuft of a papilla. It is not impossible that the Malpighian glomeruli may originate as papillary excrescences from the cœcal ends of the uriniferous tubes. (?) (*Cf. Henle,* Handbuch d. Systemat. Anatomie, Braunschweig, 1862. Eingeweidelehre, p. 310, *a*, *b*, figs. 237, 238.)

Fig. 109.



Vertical section through the skin of the lower lip (after *Thiersch*). *a.* Horny lamina of the epidermis, which is continued into the hair-sacs as the inner root-sheath; *b.* Sebaceous glands; *c.* Sweat-gland; *d.* Vessels; *e.* Papillæ of the roots of the hair.

toses to the epidermis and papillary body under a common law.

§ 287. We include the large assemblage of these superficial dermatoses under the name of eruptions, *exanthemata.* Every exanthem begins with hyperæmia of the papillary body. This is the first sign we have that the part is being irritated; it is the starting-point of all the subsequent excesses and abnormalities in its nutrition. Even at this early stage, we are struck by the contrast between the manifold variety of the coarser anatomical appearances, and the monotonous uniformity of the microscopical alterations. The major part of general dermatology may be legitimately considered as so much morbid anatomy. There is nothing to hinder the anatomist from describing and distinguishing the various naked-eye appearances, sizes, and positions of the maculæ, papules, bullæ, pustules, &c., quite as elaborately as the professed dermatologist. Pathological histology however knows nothing of all this diversity; here, as elsewhere, it shows from what simple elements nature can procure the most complex results. It recognises, strictly speaking, only two sets of morbid changes, which, either singly or in combination, make up the various exanthemata. These elementary categories may be designated as the "simple inflammatory" and the "hypertrophic inflammatory," the latter serving as a convenient transition to the simple hypertrophies of the papillary body, such as warts, &c. These divisions coincide very fairly with those based on the time which each disorder requires to run its course; thus the simple inflammatory may be called rapid or acute, the hypertrophic inflammatory slow or chronic, while the non-inflammatory hypertrophies include those forms which seldom get well if left to themselves. We must bear in mind however, that the terms "acute" and "chronic," as we now use them, are not synonymous with the same terms as employed by dermatologists; that *we* refer only to elementary lesions, and that an exanthem, which might justly be included in the chronic category of dermatologists, may really be made up of continual repetitions of an acute inflammatory process. It is desirable to guard against such misconceptions from the first. Even at the risk of saying the same thing twice over, we will narrow or extend the limits of the fundamental types of exanthematic inflammation so as to make them agree with those employed in cutaneous pathology, and leave it to our readers to simplify matters farther by means of such abstractions as have just been hinted at.

§ 288.—1. *The erythematous exanthem.* Simple erythema, even when it amounts to a positive turgescence of the cutaneous capillaries, would hardly be supposed likely to afford materials for histological investigation, were it not for the recent observations of *R. Volkmann* and *Steudener* (Centralblatt, 1868, 36) on erysipelas; these observers prove that in the course of this essentially erythematous inflammation of the skin there occurs a very extensive migration of leucocytes into the cutis and subcutaneous areolar tissue; true, these leucocytes disappear in two or three days by disintegration and absorption; still, they serve to show how easily a simple erythema may pass into those higher grades of inflammation, which it invariably precedes. Moreover, even a transient erythema usually leaves some vestiges of its presence behind it. It is usually followed by a desquamation of the outermost layer of the epidermis, whether branny (*desquamatio furfuracea*) or foliaceous (*desquamatio membranacea*). This phenomenon can only be explained by the close connexion which subsists between the nutrition of the epidermis and the changes occurring in the papillary body. Every hyperæmia involves a disturbance, an interruption in the nutrition of the epidermis. The details of this are not known. So much seems certain, that this disturbance causes a separation of the epidermis into an outer, less nourished, and an inner, better nourished layer. This separation manifests itself as a real though imperfect cleavage, or rather loosening of the substance of the cuticle between its horny and its mucous strata, without the intervention of exudation. When in the course of growth the oldest portions of epidermis come to be shed, a simultaneous detachment of the deeper and younger layers of the horny stratum bears witness to their premature death and consequent separation from their native soil.

We distinguish between diffuse and circumscribed erythemata. It often happens that an erythema which is at first diffused, becomes concentrated in course of time at one or more points of the cutaneous surface which lie within its area ; and in proportion as this occurs, we may anticipate further changes of an inflammatory kind at these points.

§ 289.—2. *The papular exanthem.* By a papule we understand a slight elevation of the cutaneous surface, which feels like a little solid nodule seated on the skin. The papule originates by the passage of an inflammatory hyperæmia into exudation, within a limited area of the papillary body. The exudation is not situated in the epidermis. This stretches unaltered over the enlarged papillæ ; it is more tense and elastic than usual owing to its extension over a larger area. The exudation is situated in the substance of the papillæ. They are saturated with an abundant supply of nutrient fluid—not with cells (at least in recent cases). We shall find hereafter that formative changes are superadded when the papule has lasted for some time, and especially if it proceed to become a pustule. The individual papillæ are markedly enlarged. It has been asserted that they undergo, not so much an elongation and thickening at their apices, as an expansion at their bases, so that the level of the surface is in some sort depressed within the area of infiltration. This assertion hardly admits of proof or disproof, inasmuch as any direct observation is as good as impracticable. For, like many other infiltrations of the connective tissue, this infiltration disappears during or immediately after death. The elastic reaction of the stretched cuticle drives the exuded fluid back into the vessels as soon as the cessation of the *vis a tergo* allows it to do so. We find patches of skin which, a short time before, exhibited the eruption in all its distinctness, apparently quite healthy. For my own part, I believe that the sharply circumscribed character of the papular elevations points rather to a turgescence of the slightly bulbous tips of the papillæ. The affection is very prone to select the ring of small, closely-set papillæ which surrounds the orifices of the hair-follicles. Such papules are circular in outline, of considerable size, and perforated at their centres by a hair. *Hebra* assumes that in these cases a minute quantity of fluid is previously exhaled between the horny and the mucous layers of the epidermis. Here too I must say that I failed to discover any fluid in the substance of the epidermis ; but the point does not seem to me of much moment.

Most papules are redder than the surrounding skin; this is no more than might be expected, since the formation of a papule is preceded by a concentration of the hyperæmia at the affected point; the occurrence of exudation however, tends to check the hyperæmia by taking up the available space, and so squeezing out the blood—the only constituent of the papilla which is free to escape. Thus it may happen that the papules are not redder than the surrounding surface, but of the same colour, or even paler.

Papular eruptions are most common in connexion with measles.

§ 290.—3. *The wheal* stands in close anatomical relationship to the papule. Wheals (*pomphi*) are broad and flat elevations of the skin, firm to the touch, as may readily be perceived by passing the hand lightly over them. The smaller wheals, those no bigger than a lentil, are circular; larger ones, often of very great size, are produced by the confluence of the smaller ones and accordingly exhibit the utmost irregularity of outline. The smaller wheals are of the same colour as the surrounding skin; they are seldom redder. The larger however and especially the more raised the wheal is, the more does its redness appear to be pushed to one side and concentrated in a narrow band along its edge, while its central part grows more and more pale. Finally we may have white wheals with a red areola. These may be regarded as the highest stage in the development of the urtical exanthem.

The wheal is an acute inflammatory œdema of the papillary body. The exudation is thinner and more serous than in the case of the papule; hence too, the rash is so very fleeting, that it may readily be increased by scratching, while it quickly fades without any trace, if left to itself. The seat of the infiltration has been already indicated. In the higher degrees of pomphosis the papillary body is swollen to such an extent that the flow of blood through it is completely arrested; the blood which is meant to supply the part is retained at its periphery, where it accumulates. The red areola of the white pomphus is therefore due to collateral hyperæmia resulting from the impermeability of the capillary networks in the interior of the swollen region.

Pomphosis, as a transient œdema of the papillary body, interferes less with the nutritive processes in the skin than any other exanthem; it is never followed by any more profound disorder; seldom even by branny desquamation of the cuticle.

Among the external irritants best adapted to produce this eruption are the sting of the nettle and that of some insects; among internal ones certain articles of diet (strawberries) and the specific cause of nettle-fever (Nesselfieber).

§ 291.—4. *The vesicular or bullous exanthem.* The papule and the wheal showed us the exudation arrested in the perivascular connective tissue, on its way from the capillaries of the papillary body to the surface of the skin. The vesicle or bulla takes us a step farther. The exudation is now in the substance of the epidermis; it accumulates between the mucous and the horny layers; the latter is raised and arched outwards like a knob. The terms "vesicula" and "bulla" are both employed to designate this condition; their difference is one of degree only. The vesicle includes those which are not bigger than millet-seeds; the bulla includes all which exceed this size.

A vesicle may be broadly said to originate in the transudation of a fluid from the vessels, which forces its way up from the distended capillaries of the papillary body, passes through the rete mucosum, and is arrested by the horny lamina. The cells of the latter are so firmly united, partly by the close way in which they are packed together, partly too by a sort of sutural connexion of their channelled surfaces, that they form a continuous tough membrane, impermeable to fluid, and well adapted for retaining and roofing in even larger quantities of it. The mucous layer is variously affected in different cases. If a bleb is developed very rapidly, as *e.g.* in gangrene, the soft bodies of the cells are mechanically stretched into slender threads by the force of the transuding current—threads which give a mossy roughness to the surface of the papillary body. Should the transudation take place more slowly, as in Herpes and Erysipelas bullosum (*Haight*), the deepest layer of the rete Malpighii remains unaltered, while the "intermediate" epithelium-cells are partly detached, partly pushed aside. The transuded fluid wells up with greater force from the apices of the papillæ than from the interpapillary furrows; hence the layer of cells above alluded to is stripped from the papillæ, while remaining attached to the bottom of the furrows. A system of cellular membranes and trabeculæ is thus formed; these structures extend more or less vertically across the interval between the horny layer and the papillary body; the thickest ones spring from the interpapillary fissures; they grow more and more slender in proportion as they recede towards the summit of the papillary elevations. These trabeculæ are all made up of nucleated "intermediate" cells, which have been stretched and flattened out mechanically. The thinnest bands consist of single cells, often drawn out into several processes. If the transudation is more copious, the trabeculæ, whatever their size, are torn across, one-half adhering to the detached horny layer, while the other is retained by the papillary body.

It is only in miliary vesicles that the fluid is contained between the layers of the horny lamina (*Haight*); but the intimate connexion of this exudation with the perspiratory secretion makes us hesitate before reckoning miliaria among vesicular eruptions at all. The fate of the vesicles is different in different cases; they may burst and discharge their contents, or they may remain stationary until the hyperæmia remits and allows the exuded fluid to return to the blood. The pressure of the stretched horny lamina, whose elasticity is well known, may contribute to the latter issue. That this force ought really to be taken into account, is plain from a consideration of blebs with a hyperæmic areola. In these, the contents of the bleb compress the underlying vessels to such an extent, that the afflux of blood is checked, and stagnation consequently occurs at the margin of the bleb. The strata of epidermis which have once been separated cannot however reunite. Even when the horny lamina is closely applied to the underlying stratum, and the *status quo ante* has apparently been re-established, we still find that the affected lamellæ wither and are shed before their time. Meanwhile a new horny lamina is developed at the expense of the rete Malpighii. This continues abnormally thin for a long period; the vessels of the papillary body shine through it so brightly that the size and shape of the former bleb may be recognised for weeks and weeks as a red spot.

The histological details of this renewal—what part of the papillary body is mainly instrumental in the process, how stratification is produced, &c.—all these are questions which normal histology must answer; it has not answered them yet. This issue is known as "desiccation of the bleb:" it has to be distinguished from another and less favourable one, which may be briefly called "suppurative metamorphosis." This trenches however on another department of our subject.

Vesicular and bullous eruptions are extremely common; they are caused by external and internal irritants of all sorts. Among the former may be enumerated heat, blisters and epispastic fomentations, mechanical irritants, scratching, and recurring pressure; among the latter, Herpes, Pemphigus, Measles, &c.

§ 292.—5. *The pustular exanthem.* The term "pustule" is summarily employed in dermatology to denote every circumscribed accumulation of pus under the epidermis. Accordingly the pustule is a sharply-defined straw-coloured elevation; and if we add that it is always circular, often provided with a central depression or umbilicus, and girdled with a red areola, we shall have gone far to exhaust its denotation. Now it is obvious that such accumulations of pus may arise in the most diverse ways; and this qualifies the value of the above definition. We set aside for the present such pustules as are due to suppuration in the deeper parts of the skin (*e.g.* round hair-sacs) and confine our attention to those two varieties in which the starting-point of the suppuration does not extend below the level of the papillary body.

a. We have just seen that pustules may originate from vesicles; this occurs in Eczema, Impetigo, Herpes, Pemphigus, and Ecthyma. We may observe the gradually increasing turbidity of the vesicular contents even with the naked eye: by subjecting a drop of the contained fluid to microscopical examination we may convince ourselves that the opacity is due to the presence of detached epithelial cells and numerous pus-corpuscles. At a later stage, the pus-corpuscles predominate; and when the process has reached its height, we are quite justified in summarily calling the contents of the vesicle a rather thin and fluid pus. A vertical section through the skin (fig. 111) shows the outline of the papillary body in a state of good preservation, but with its substance permeated by a large number of young cells which accumulate at the apices of the papillæ to such an extent, that at these points a layer of such cells extends uninterruptedly to the deepest stratum of the rete Malpighii. This can still be recognised on the sides of the papillæ and in the furrows between them, if we make use of the yellowish colour and erect position of its columnar cells as a guide. The state of things over the apices of the papillæ is very different. Here we can no longer distinguish any line of demarcation between epithelium and connective tissue; it is only by dissecting the parts with needles that we find it possible to say: here is the boundary of the papillæ; there begins the cuticle. For my own part I cannot doubt that this is the main source of the young cells which we find in the contents of the vesicle. The irritated papillary body is in a state of the most exuberant proliferation; the young cells travel towards the surface, where they are set free as embryonic cells and pus-corpuscles before they have time to become developed into epithelia. Some may possibly force their way through between the cells of the rete Malpighii; the majority migrate outwards from the tips of the papillæ where the rete has given way, and where the relation between the secreting surface and the secreted products is precisely the same as on a granulating surface.

The whole process is thus seen to be an *acute purulent catarrh* of the skin. If we take the preliminary vesicular stage into account we may speak of a catarrh originally serous, which has passed into the purulent stage.* Recovery from this state may take place in various ways, according to the treatment adopted. If things are left to themselves, a scab is speedily formed by the drying up of the purulent contents of the bleb; under this scab the formative actions become gradually slower, and end in the production of a new epidermic coat. The scab has been regarded by many as a sort of roof under cover of which nature could proceed undisturbed to the renewal of the epidermis. The hypothesis is as false as it is attractive. The scab is simply a mass of dead and dried organic matter, which tends to undergo further decomposition and putrefaction so soon as it is supplied with enough moisture for the purpose. If we reflect that the papillary body in its catarrhal state yields enough fluid to set this putrefactive process going, and that decomposing and therefore irritating matters are being continually produced on the under surface of the scab, the surface which is turned towards the papillary body, we cannot but conclude, and our conclusion will be justified by clinical experience, that so far from exerting any salutary influence, the scab is positively a hindrance to the reparative process; peculiarly favourable conditions, such as a very rapid recession of the hyperæmia, a very complete degree of desiccation, &c., being needed, to allow of the catarrhal process healing underneath the scab.

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* The word "catarrh" is usually employed to denote the analogous morbid conditions which occur in mucous membranes. Accordingly I shall discuss the special histology of catarrh among the diseases of those membranes.

The denuded surface is clothed in just the same way as it is after the desiccation of a vesicle. I have indeed observed that concentrically-laminated globes, the so-called "pearly nodules," are exceptionally frequent in the new cuticle produced under such circumstances; this however is undoubtedly owing to temporary irregularities in the process of stratification.

§ 293. The case is different when we have to do with an eruption which, for other reasons, has no tendency to get well; when the vesicles and pustules are merely the acute beginnings of a chronic catarrh. For instance, some forms of eczema affecting the legs are essentially due, not to external irritation, but to chronic disturbances of the circulation, to venous hyperæmia and phlebectasy.

These afford us our best opportunities for observing *chronic catarrh* of the skin. Its phenomena depend on a chronicity and increasing intensity of the hyperæmia of the papillary body. This causes in the first place, and directly, the continuance of secretion from the affected patch. Large quantities of transuded fluid force their way to the surface; the purulent character of this secretion standing in an inverse ratio to its volume, since the rate of production of the pus-corpuscles remains constant, while the transudation increases considerably in amount. Finally we get a fluid which is almost clear, and very rich in salts and albumen; its enormous quantity sets all bandages at defiance ("Salt Flux"). The skin undergoes a progressive alteration which may briefly be described as an inflammatory hypertrophy. This is also due to the hyperæmia of the papillary body; at least it is always the papillæ which begin by growing at the expense of the embryonic tissue produced at their apices, just as happens in the growth of granulations. We may occasionally observe, even with the naked eye, little red buds sprouting up, which exhibit all the histological characters of granulations, but which are merely the enlarged—or, if the term be preferred—the degenerated papillæ of the skin itself.*

§ 294. As the disease progresses, the state of irritation which was originally confined to the surface, extends to the deeper layers of the skin, to the cutis and subcutaneous areolar tissue. This serves to connect chronic catarrh of the skin with those conditions which are described under the name of Elephantiasis in the second part of the present chapter. It is difficult to determine how far this may depend on the catarrhal irritation of the surface, in what measure it may be considered as a reactive hypertrophy; and what share belongs to the predisposing cause of the eczema itself, to the disturbance of the circulation of the blood and lymph, and how far therefore the morbid changes deserve to be regarded as an independent disease; I will therefore break off the thread of my exposition at this point and take it up again when I come to treat of Elephantiasis.

At present I will only speak about the tendency towards recovery, and the actual process of repair, in chronic catarrh. We have traced a close analogy between the papillary body in its catarrhal state and the surface of a granulating wound; the analogy may be extended to its mode of healing, which closely resembles that of repair by the second intention. The phenomena exhibited by the cutis must be viewed as analogous to that "*cicatrisation from below*" which, as the reader may recollect, plays so momentous a part in repair by the second intention (cf. fig. 39, *c*, § 104). These phenomena consist of a very curious combination of two processes which act in opposition to each other, viz. the production of cicatricial tissue, and an increase instead of a diminution in volume. We shall have to return to the consideration of this point under the head of Elephantiasis. It cannot be doubted that these phenomena react upon the state of the surface; on examining vertical sections (fig. 110) we often find the remains of obliterated vessels, recognisable as pigmented striæ, mounting obliquely towards the dermal surface; we may legitimately infer that their obliteration must have hindered the supply of blood to the papillary body. It would however be a great mistake to ground any hopes of the healing of the affected surface on these processes in the cutis, as in the case of repair by the second intention. On the contrary, everything depends on the treatment to which the diseased part is subjected. Nature must be helped by astringent and siccative remedies, but chiefly by a systematic application of pressure. Under such conditions recovery takes place by a gradual recession of the proliferated papillæ, and a skinning over of the entire surface. The diminution in size of the papillæ is operated partly by the return of the infiltrated fluid into the blood, partly by the fatty degeneration and absorption of large numbers of corpuscular elements. Intercellular substance appears between the cells; hairs, glands, and nerve-fibres are no longer to be found; they have obviously perished in the stormy activity which prevailed in the connective tissue around them: but nothing is known about the way in which they are destroyed. The papillæ never reach their normal height; in fact it is only the shallow undulations of the boundary-line between connective tissue and epidermis which indicate their existence (fig. 110).

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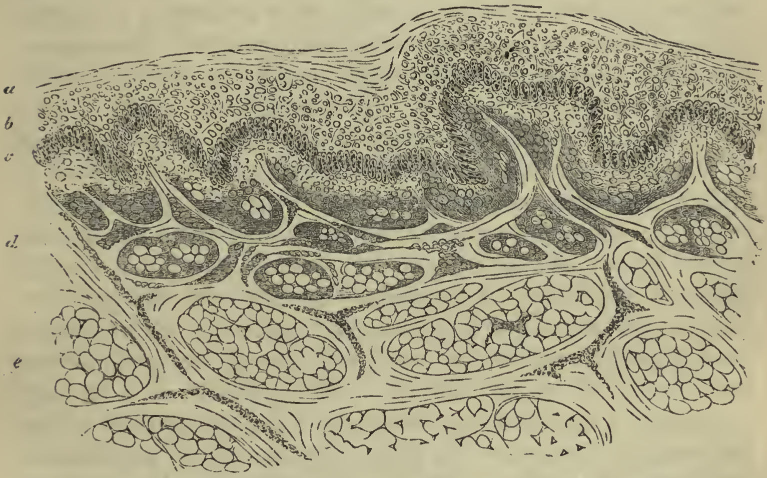
* This illustrates very strikingly the close connexion between hyperplastic and heteroplastic evolution. Those who are inclined to distinguish sharply, not merely between hyperplastic and heteroplastic growth, but between inflammatory heteroplasia and heteroplastic tumours, between simple and inflammatory hypertrophy, will do well to take this lesson, which skin-diseases offer, to heart. We may and ought to avail ourselves of these definitions for the purpose of giving clearness to our conceptions of the phenomena, but we must beware of elevating them to the rank of rigid formulæ. None such exist in nature, which reconciles all contrasts. In the present case, the development of embryonic tissue at the junction of the epidermis with the connective tissue, belongs, up to a certain point, to the normal plan of evolution of the skin; no sooner however does it overstep this limit, than it at once converts the cutaneous surface into a granulating sore.

In marked contrast to a granulating sore, the skinning-over of the surface starts from several centres at once; it proceeds from within outwards as well as from without inwards; this anomaly is due to the presence everywhere of remnants of the old rete Malpighii, which may proceed directly to the formation of a new horny lamina. The horny layer continues very thin for a long time, and we know how easily a renewal of the flux may rupture the delicate membrane and so re-establish the disease as soon as it is cured. It is worth notice that in cases of permanent recovery the deepest cells of the rete Malpighii exhibit a striking tendency to become infiltrated with pigment (fig. 110); this manifests itself to the naked eye as a brownish staining, diffuse or circumscribed, of the affected patch of skin.

§ 295.—*b.* The second variety of exanthematic pustule—*the pock*—is undoubtedly the most interesting of all cutaneous eruptions from a histological point of view. The pock is at one period of its existence a simple pustule, but that is before it has attained maturity; moreover it arrives at this stage by so peculiar a road, that it is entitled on both grounds to an independent position.

Fig. 110.



Vertical section through the skin after chronic eczema. *a.* Horny lamina; *b.* Mucous layer of the epidermis; *c.* Pigmented layer of columnar cells; *d.* Papillary body; *e.* Cutis traversed by streaks of pigment.

The pock originates as a papule on a very hyperæmic base. This proposition, which is repeated by all text-books, may be allowed to pass unchallenged, if we choose to term every hard, nodular elevation of the cutaneous surface a papule. But it must be remembered that the small-pox papule differs very essentially from the papules we have already described (*e.g.* the papule of measles). The small-pox papule is situated, at least in great part, *in* the substance of the epidermis, not underneath it. It begins, apart from the hyperæmic condition of the papillary body, as a circumscribed "parenchymatous inflammation" of the epidermis. I use this word under reserve. That peculiar cloudiness and swelling of the cells which was discussed in §§ 36 and 37, and which meets us here once more, has not in my opinion established itself on a very firm footing, as yet, in general pathology. The circumstance that the swelling leads as often to fatty degeneration as to endogenous multiplication, renders it doubtful whether it ought to be considered as a progressive or as a retrograde metamorphosis of cells. The present case is undoubtedly one of incipient productive activity, which may therefore rightly be called "inflammatory."

It is neither in the deepest nor in the most superficial layer of the epidermis that the swelling begins; its starting-point is in the middle stratum, which we have already described as composed of "intermediate cells," and as belonging to the mucous layer. These cells are no longer naked, like those smaller elements which are in immediate contact with the papillary body; they possess a membranous investment whose surface already exhibits here and there that delicate grooving which was first discovered by *M. Schultze.* The presence of a limitary membrane renders it impossible for them to respond to the inflammatory stimulus by simple fission; their proliferation must take place by endogenous development. But the first stage of endogenous growth is that same "cloudy swelling" which is followed by segmentation of the enlarged protoplasm and the transformation of the "segmentary spheres" into pus-corpuscles (cf. the description in § 68, fig. 30).

§ 296. The shape of the individual pock is always circular; more complex forms are always due to the confluence of adjoining papules. This peculiarity, as may be shown in the case of many pocks, is due to a concentric arrangement of their elements round the orifice of a hair-sac or sweat-gland. These pocks may be distinguished from the rest even with the naked eye. They exhibit a central depression, the "umbilicus." Everybody knows that both the rete Malpighii and the horny layer of the epidermis are prolonged into the hair-sacs. Now if the swelling — or still more that serous saturation of the rete Malpighii of which I am about to speak—extends to the circumference of the follicular orifice, then the horny epidermic lamina which lines the follicle (the inner root-sheath) will act upon the enlargement as a central retinaculum (or bridle); and will thus prevent the middle of the pock from rising to the same height as its periphery. The epithelium which lines the ducts of the sweat-glands is less tough than the inner root-sheath of the hair-sacs. It owes what cohesive power it has to its being stratified in a plane which cuts that of the cuticular strata at right angles or obliquely. But the morbid change does not even involve the parts in immediate contact with the duct. At all events I have many specimens in my possession which exhibit the ducts of sweat-glands with the tissues immediately surrounding them as the retinacula of smallpox papules (fig. 111, *a*).*

§ 297. The next step in the developmental process is the conversion of the papule into a pustule. This is invariably preceded by a serous infiltration of the epidermis. A clear fluid forces its way up from the papillary body, and raises the horny lamina of the cuticle; it does not detach it from the mucous layer as in the production of a vesicle, but forces itself between the lamellæ of the latter structure, pushing them asunder, and displacing them to such an extent, that from having been horizontal they come to occupy an oblique or vertical position (fig. 111, *b*). This gives the upper part of the pock a chambered appearance, which has long attracted the notice of pathologists and has induced many to ascribe a loculose structure to the entire pock. This is decidedly incorrect. It is only the upper portion, the "dome" of the pock, which is chambered. It is from this that we are able to obtain, either by a series of fine punctures, or by a single shallow horizontal incision, which separates only the horny lamina, that clear lymph which plays so important a part in the propagation of cow-pox.

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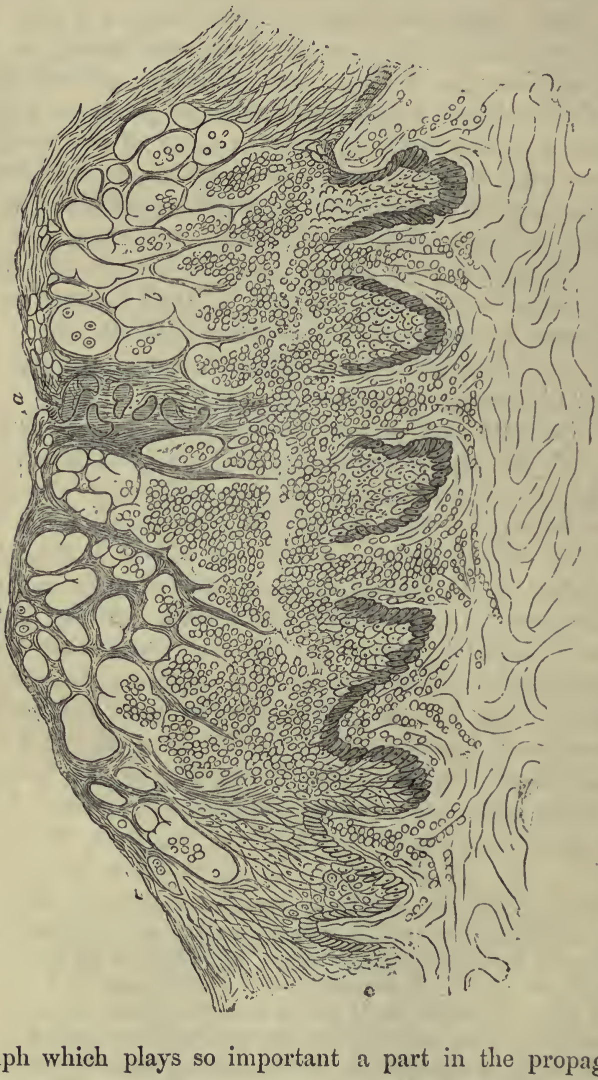
* *Auspitz* and *Basch* (*Virchow's* Archiv xxviii.) explain the umbilication of the pustule in a way which does not seem to me very plausible: "The swelling of the individual cells keeps extending in all directions from the affected centre; consequently the efflorescence as a whole, increases in bulk; the formation of pus in its centre proceeds but slowly at first, and the pus is enclosed by the peripheric accumulation of swollen cells as by a capsule; the latter growing continually larger, without the pus-formation in its interior being able to keep pace with it."

Fig. 111.



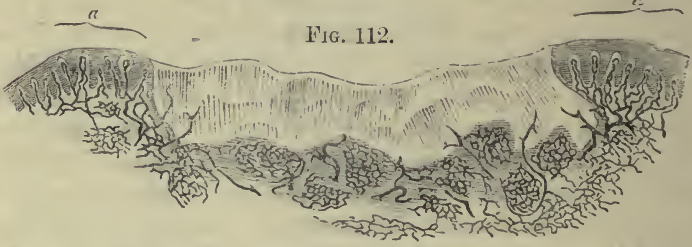
Vertical section through the middle of a pock passing from the papular to the pustular stage. *a.* Umbilicus with duct of sweat-gland; *b.* Loculi in the substance of the epidermis, formed by the separation of the lamellæ and filled with lymph; *c.* Smallest loculi, containing single pus-cells. The papillary body in a state of purulent catarrh. $\frac{1}{200}$.

§ 298. Suppuration now sets in in the deeper layers of the epidermis, where it follows immediately upon the parenchymatous inflammation. A host of pus-corpuscles is generated by each of the swollen cells, and the chambered dome of the pock is soon filled with a yellowish purulent fluid in place of the transparent lymph which it previously contained. The pus-formation need not go beyond the epithelium. The pus dries up, and before the pock is thrown off, a new epithelial covering for the cutis is completed underneath it.

As a rule however, the papillary body takes part with the epithelium in the production of pus. It may do this in two ways. We may distinguish between a catarrhal and a diphtheritic pus-formation. For the catarrhal variety I may refer the reader to § 292 and fig. 111. The suppuration is superficial, the papillary body remains intact, and is roofed in during convalescence by a layer of new cuticle which long continues thinner than the normal epidermis. This variety of pock heals without leaving any scar. Both anatomically and clinically it is a far less serious affection than the "destructive" pock. The latter consists, not in a mere secretion of pus from the papillary body, but in a liquefaction of its proper substance; hence it results in loss of tissue, in ulceration and scarring. *Bärensprung* has given an excellent description of the naked-eye characters of the diphtheritic pock, as follows: "In the second stage (of pock-formation) an exudation takes place wherever simple hyperæmia existed; those portions of the cutis which hitherto presented a lively redness, now assume a white colour which extends to the subcutaneous areolar tissue; they seem impregnated with a soft mass of exudation; their edges are surrounded by a red areola; the papillæ too have lost their colour. In the third stage, the vesicles undergo conversion into pustules. On investigating the pock at this period, we can assure ourselves that all the infiltrated part of the cutis, together with its papillæ, has been destroyed by suppuration. The pock exhibits a hemispherical, vaulted appearance, and contains, besides pus, shreds of the necrosed tissue. A fourth stage exhibits the pustules torn open at their apices, and emptied of their contents; their place is taken by little open ulcers, which leave the well-known reticulated scars behind them when they heal."

The microscope furnishes us with a very simple and thoroughly explanatory commentary on this succinct and luminous description. *Bärensprung's* exudation is not something amorphous—not coagulated albumen or fibrin; it is made up of corpuscular elements—of pus-cells. We must recollect that even in the catarrhal variety of suppuration, the papillary body was abundantly permeated by young cells, some portion of which emigrated and were thrown off. In the present case, this infiltration is excessive in amount; the cells accumulate in such enormous numbers in the interior of the papillæ, that they not only mask, but compress, and so cause atrophy of all the other structures, the connective-tissue fibres, the vessels and the nerves. The blood cannot gain access to the infiltrated part; hence its pallor. The annexed drawing (fig. 112) shows this state of things tolerably well. The vessels have been injected with gelatine and carmine.

FIG. 112.



Diphtheritic pock. *a*. The normal skin surrounding it, which is successfully injected. For further details *see* text. $\frac{1}{50}$.

Wherever the blood failed to penetrate during life, the injection has also failed to enter; so that to right and left of the pock we see the capillary loops of the papillæ well filled (*a a*), while the pock itself contains no trace of them. It looks as if a semicircular piece of the cutis with its papillæ had been cut out of the capillary network. The whole of this portion is infiltrated with pus-corpuscles in the way described above, and may be regarded as already dead; the only question is how long the fibres of the connective tissue, and the obliterated vessels which it contains, and which connect it with the neighbouring parts, will resist disintegration. They last longer in adults than in young people. In the former case an adherent slough is formed *in* the cutis; in the latter, the infiltrated part soon melts into pus; this dries into a crust; in either case however a superficial defect of the cutis remains—an ulcer—which heals by the second intention, and leaves a permanent scar.

§ 299.—6. *The squamous exanthem.* I have referred on more than one occasion to the difficulties which beset our path whenever we try to separate the conception of inflammation from that of hypertrophy, as ætiological categories of morbid growth. The squamous exanthem undoubtedly originates in a chronic inflammation of circumscribed portions of the skin. These are reddened, slightly swollen, and endowed with all the other attributes of inflammatory hyperæmia; the result of this hyperæmic condition being, not an exudation into or under the epidermis, but merely an over-production of perfectly normal epidermic elements. This begins as an increased desquamation of horny cells, of "cuticular scales," upon the hyperæmic, slightly raised patch of skin (*squamæ*, *desquamatio*, squamous exanthem). The secretion of cells however, soon assumes greater proportions; white masses varying in size from a millet-seed to a lentil, and also discoidal plates, are formed, consisting of scales heaped up on one another, and firmly adherent to the parts beneath them (Psoriasis). Why, as the disease progresses, the epidermic cells cease to be simply cast off, why they should accumulate in thick scales, is elucidated by pathological histology as follows. The more exuberant the production of cells on the surface of the inflamed cutis, the more imperfect is the degree of development attained by each individual cell. The average height to which their development proceeds under such circumstances is that of the "intermediate cells," between the cylindrical elements of the mucous layer and the deeper cells of the horny lamina. That systematic hardening which we call "cornification," remains in abeyance; in its place we have a simple desiccation of the soft protoplasm. During this desiccation the cells very naturally adhere to one another, and thus retain their connexion (which is purely mechanical) with the surface of the body for a longer period.

The silvery hue of the scales in psoriasis is due to the admission of air into their substance, simultaneously with the desiccation of their cells; and this also gives them their peculiarly spongy and porous consistency. If we pick off the mass of scales, which may be done as a rule without employing much force, we find the papillary body under it almost entirely bare. The layer of epithelium which protects it is so thin that the least touch is enough to detach it, and to make the surface bleed: we must recollect notwithstanding, that the continuity of the epithelial layer is still quite unimpaired, and that there is no trace of any exudation. Taking all these circumstances into account, we can arrive at only one conclusion with regard to the essential nature of the squamous exanthem, viz. that it is a morbid growth taking place upon a decidedly inflamed base; and that this growth exhibits a very marked excess of, but—apart from the imperfection of the cornifying process—no qualitative deviation from, the normal course of cuticular development. The squamous exanthem is an inflammatory overgrowth, and serves, as such, to connect the foregoing sections with the ensuing one.

β *Hypertrophy.*

§ 300. What has been said above (§ 83) with reference to the physiological growth of epithelium and the extent to which the subepithelial connective tissue takes part in the process, may be transferred directly to the epidermis and papillary body. The papillary body supplies the epidermis with young cells: these are added to the rete Malpighii and gradually develope into epidermic cells. A morbid over-activity of this process forms the common basis of a great number of hypertrophic conditions, which we are now about to consider. I say "a great number," and I attribute the manifold variety of the appearances presented, to the circumstance that the embryo-cell which ultimately becomes an epithelial cell, is, before its emigration from the connective tissue, one of its homologous constituents, and is equally capable of contributing to the overgrowth of the papillary body, when it is produced in abnormal quantities. The very process which ultimately issues in the formation of epithelial cells, if it be interrupted at an earlier stage, must inevitably produce connective tissue. In including the overgrowth of the epidermis and papillary body in one and the same chapter, I have therefore been guided, not merely by the circumstance that they are in fact nearly always associated in nature, but also by the unity of the fundamental process which underlies them both. The series opens with those forms in which the epidermis alone is affected; it ends with those which are limited to the papillary body; the intermediate forms being arranged according as one or other constituent is chiefly involved, the middle term corresponding to the equal implication of both.

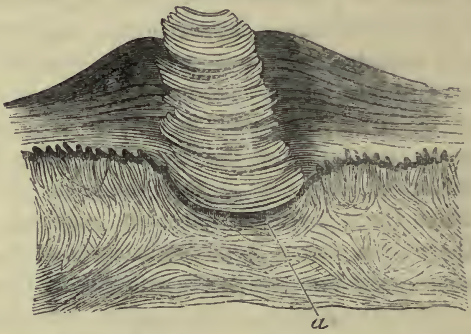
§ 301.—THE CALLOSITY (*callositas*) is a circumscribed thickening of the horny layer of the epidermis. It forms a flattened superficial elevation of horny transparency, which slopes gradually down on every side. Its consistency depends on the amount of moisture present, and varies from the elastic and flexible to the horny and brittle. In its minute characters it differs from the normal structure of the horny layer, only in the number of superimposed strata of flattened and horny epidermic cells.

If it be the function of the epidermis to protect the surface of the body from external influences by a coating which, however thin, is nevertheless very resistant, we may legitimately regard the callosity as a functional hypertrophy, analogous to the hypertrophy of muscles from over-work. Observation tells us that callosities are exclusively produced at such points of the cutaneous surface as are exposed to severe or often-repeated pressure; as *e.g.* the palm of the hand and sole of the foot. We should then ascribe the greater thickness of the horny layer, with which these parts are naturally endowed, to natural selection. The notion that a hyperæmic state of the papillary body, and a consequent increase in the nutrition of the epidermis, are caused by external pressure on those parts, is far simpler; and so far from being antagonistic to the former view, it rather serves to explain it.

§ 302. THE CORN (*clavus*) is a modified callosity. Here too, external pressure acts as the efficient cause of the overgrowth. The difference in the results depends on a variation in its mode of action; if the point at which the two opposing forces come into collision coincides accurately with the point of contact between the compressed part and the compressing agent, a callosity is produced; if on the other hand the two points do not coincide, if the seat of conflict is withdrawn into the interior of the compressed part, in other words if the compressed part is capable of yielding to the pressure, a corn results.

Fig. 113 represents a vertical section through a corn under a magnifying power of 20 diameters. Here too we have a trifling elevation of the surface; it is, however, far smaller and more circumscribed than in the case of the callosity. The swelling which proceeds from the under surface of the thickened horny layer at this point, is of far greater moment (*a*). This forms a truncated cone with its axis at right angles to the surface of the skin, into which it has penetrated for some distance. Its pressure has flattened the papillary elevations; the cutis itself is beginning to get thinner, and cases not unfrequently occur in which it is actually perforated. On turning our attention to the epidermis itself, we notice a striking departure from the usual plane of its stratification where the corn is thickest. For, coinciding with and exactly parallel to the curvature of the conical plug which is forcing its way into the cutis, all the superjacent strata of epidermis are bent with their convexity inwards, so that the centre of the corn is in some sort differentiated from the parts around it. This inward curvature is also due to the external pressure; which may be said as it were to have manufactured a tool for itself out of the epidermis, with which it can proceed to operate against the deeper parts of the skin.

FIG. 113.



Vertical section through a corn (after *Simon*). The papillary body at *a* is seen to be flattened by the pressure of the central part of the corn. $\frac{1}{20}$.

§ 303. The KERATOSES of *Lebert* form a comparatively rare, but all the more interesting group of thickenings of the horny layer of the cuticle. Monstrous accumulations of horny matter on the surface of the skin are rendered possible in the keratoses, by the fact that the stratification of the horny cells of the epidermis follows a different law from that by which it is normally governed.

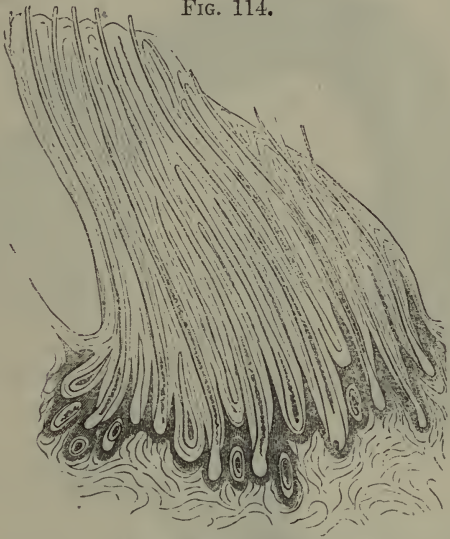
It is well known that under ordinary conditions, the strata of horny cells lie parallel with the surface of the body, and that the papillæ take no part in the finer subdivision of the cutaneous surface. It is only the deepest layer of cells forming the rete Malpighii, which accurately follows every elevation and depression; and which would therefore present, if taken by itself, a perfect mould of the papillary body. Between this and the horny layer is interposed the thick cushion of the "intermediate cells;" these are not stratified, and therefore furnish materials which are, from this point of view, quite neutral, for filling up all the inequalities of the layer below them, and so paving the way for the horizontal stratification of the layers above them. In the keratoses these "intermediate cells" are either quite absent or else disproportionately few in number. To the best of my belief they become prematurely horny, and this I regard as the essential physiological basis of the entire disorder. The absence of "intermediate cells" necessarily entails the absence of any transition from the one plane of stratification to the other: the horny layer of the epidermis is obliged in consequence to follow the rete Malpighii in its adaptation to all the elevations and depressions of the papillary body. Each layer of horny cells must therefore send into the layer which lies immediately above it, processes exactly resembling those which it receives from the layer immediately below it; processes which correspond exactly to those which the papillary body projects into the deepest layer of the horny stratum. All the constituent layers are thus indissolubly united; hence all the horny matter remains where it is produced; hence too the possibility of those extraordinary thickenings of the horny lamina which characterise the entire group of keratoses.

§ 304. Following *Lebert*, we distinguish a diffuse from a circumscribed form of keratosis. The former results in the production of flat, horny scales, which often cover large areas of skin. Not unfrequently they resemble the scales of fishes; hence the name *Ichthyosis;* occasionally they assume a more protuberant, conoidal or prismoid form, thus approaching the circumscribed variety of keratosis, the *cornu humanum.* That the great bulk of these scales is made up of horny cuticular cells is beyond doubt; some authors indeed allege that they have succeeded in isolating fibres and lamellæ, by teazing out the scales after maceration; but these fibres and lamellæ must also have consisted of epidermic cells. The mode of their occurrence will be self-evident from the ensuing observations.

If we break an ichthyotic scale in two, we may detect a vertical striation on the fractured surface; here and there too, something like stiff fibrils may appear to project. By macerating the scale in feebly alkaline liquids, and then treating it very cautiously with needles, shaking it, &c., we may now and then succeed in breaking it up entirely into vertical prisms, or, if the term be preferred, into short and thick fibres. Every one of these fibres may be shown to consist of a certain number of horny lamellæ concentrically grouped round a central axis; when cut across, they may be counted on the cut surface like the annual rings of a tree. In the axis of the upper two-thirds of each pseudo-fibre we find nothing; in the lower third we find, either nothing at all, or a minute cavity which was once occupied by a more or less elongated papilla of the cutis. We infer from this, that it is the papillæ which regulate the peculiar stratification of the horny lamellæ. The axis of our concentric cylinder is continuous with that of the papilla; and the almost vertical inclination of the lamellæ is merely a repetition of its steep and sloping sides.

This explanation does not cover all the phenomena of ichthyosis. We must bear in mind that the surface of the skin also presents vertical planes where it is bent inwards to form the hair-sacs; that these vertical surfaces are directly continuous with the sides of the papillæ; also, that the epithelial lining of the hair-sacs is merely a prolongation of the epidermis. Nothing is more usual than the extension of the ichthyosis to the hair-sacs when it happens to affect hairy parts of the skin. The horny lamellæ which are thus produced, form, as might have been anticipated, casts of the hair-sacs; on transverse section they exhibit concentric rings round an axial cavity. When the cavity is occupied by a hair, this appears in some sort as the axis of the laminated body; this circumstance may be made use of as a guide; but it must not lead us to imagine that the hair, as such, exerts any regulating influence upon the stratification of the horny lamellæ. The hairs upon the affected patch are thin and caducous; this points to a disturbance in their nutrition, due to the cornification of the hair-sac. The process extends as a rule, deep into the fundus of the sac; the hair-bulb proper alone remaining unaffected. Fig. 114 represents a vertical section through an ichthyotic scale, and shows its connexion with the underlying skin. The specimen was taken from a calf affected with congenital ichthyosis; it is preserved in the Physiological Institute at Breslau,* and is especially fitted to shed light on the relation of ichthyosis to the hair-sacs.

FIG. 114.



Ichthyotic scale; vertical section. Taken from a calf affected with ichthyosis. $\frac{1}{30}$.

§ 305. With ichthyosis we may associate cutaneous horns (*cornu humanum*) as circumscribed varieties of keratosis. A monster of this description (9 inches in length) is preserved in the collection of the Pathological Institute at Bonn. As the figure (fig. 115) shows, it is a rounded prism, longitudinally grooved, and spirally twisted like a ram's horn. Most cutaneous horns, though neither as long nor as thick as this one, present

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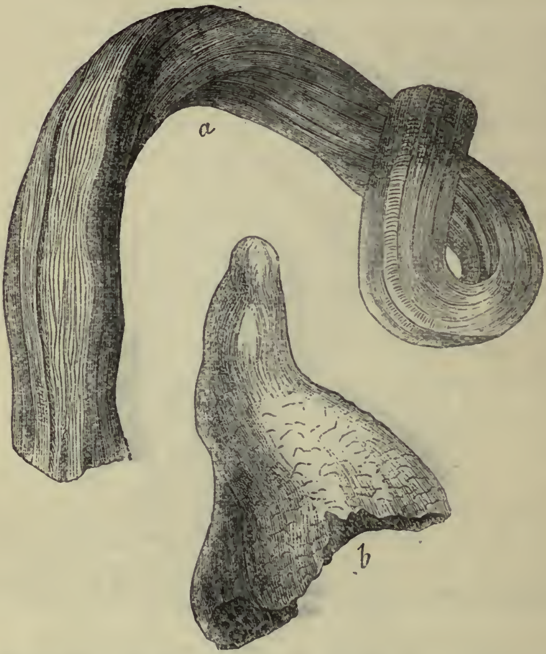
[*] Cf. *Harpeck,* description of the skin of a calf born with Ichthyosis cornea. *Reichert* u. *Dubois-Reymond's* Archiv. Jahrgang 1862. Heft iii. p. 393.

the same sort of appearance. On careful examination, each of the longitudinal grooves or furrows is found to correspond to a single cutaneous papilla—which is not always elongated; the horn as a whole springing from a group of papillæ as its base, so that in this respect its structure agrees perfectly with that of an ichthyotic scale. We meet with horns, however, which are not of uniform thickness throughout, but conical, tapering to a point. There is an exquisite specimen of this variety too in the Bonn collection (fig. 115). The rather abrupt increase in diameter as we approach the base of the horn, is due to the progressive addition of new horny lamellæ, which overlie one another in an imbricate manner. Each of these lamellæ again is made up of a series of elongated prisms, corresponding to single papillæ; it is only at the extreme periphery that we can obtain by maceration true lamellæ, which exhibit the papillary moulding in somewhat

Fig. 115.



a. Cutaneous horn 9 inches long, from the collection of the Pathological Institute at Bonn. Natural size, after *O. Weber*.
b. Another horn in the same collection, natural size.

less accentuated curves. It is clear that the process was originally confined to a smaller group of cutaneous papillæ, and spread, at first gradually, then with progressively increasing rapidity, to surrounding parts.

If we examine the under surface of one of these horns after its removal, we not unfrequently observe a number of small conical projections; these were recognised by *Virchow* to be horny casts of hair-follicles. So that here also, as in ichthyosis, the morbid process may extend to the hair-sacs. The horny matter produced by the hair-sacs can never indeed contribute to raise the level of the surface; so that it would be absurd to talk of the cornu humanum *originating* from the hair-follicles. Their implication in the process, however, induces a thickening of the horn at its base; and as this is lodged in the very substance of the cutis, it raises the notion that the horn springs from a saccular depression—a dilated follicle—of the skin. This explains much of what has been put forth concerning the follicular origin of cutaneous horns. The necessary basis for the growth of a horn is always a group of papillæ; and when we find horns springing from the fundus of a sebaceous cyst we are tempted to inquire, first, whether the cyst was really prior in point of time, and secondly, whether these horns also do not spring from a basis of proliferated papillæ. I have often seen vast numbers of small, pointed papillæ on the inner surface of sebaceous cysts, whose growth must obviously have been secondary to the formation of the cyst itself.

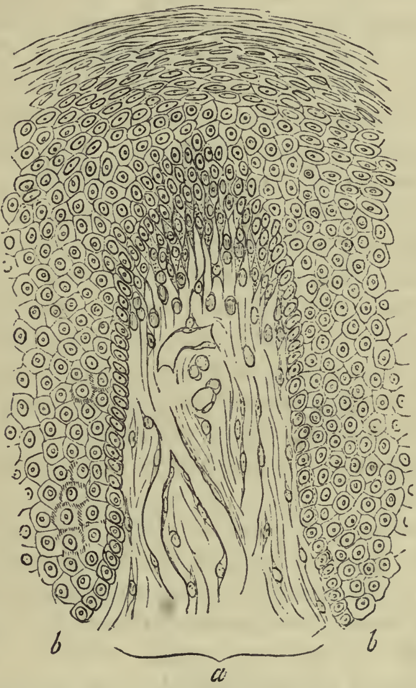
§ 306. *Appendix.*—The appendages of the horny layer of the cuticle—the hair and the nails—are, under ordinary circumstances, the largest accumulations of horny matter in a compact form, to be met with in the body. After they have once assumed their proper shape, they are not liable to any important change. At the utmost they can only undergo atrophy, *i.e.* they may split up and fall off prematurely; and even this is a result, not of any disease proper to the hair or the nails, but of some morbid condition of their matrix. The same may be said of the opposite condition of hypertrophy of the hair and the nails. Whatever points of interest these conditions may present to the histologist, will be considered, as regards the hair, in the chapter on the Hair-Sacs and Sebaceous Follicles;—and as regards the nails, at once.

ONYCHOGRYPHOSIS (*Virchow*) or the claw-like deformity of the nails which is associated with their simultaneous detachment from their bed, depends upon a hyperplastic state of the entire matrix of the nail. First stands that portion of its bed which forms the lower boundary of the onychial fold (Nagelfalz). The long, horizontal papillæ of this region furnish nearly all the substance of the nail, since this is no thicker at the finger-tip than it is at the edge of the lunula, up to which the papillæ in question extend. This gives the nail its ridged appearance, very apparent by reflected light; each ridge corresponding to a single papilla in the same way as the vertical fibres of the ichthyotic scale. Irregularities in the rate of growth, which may be alternately accelerated and retarded, give rise to transverse ridges and furrows. I have repeatedly observed that the remissions and renewals of nutritive activity during subacute pyrexial disorders leave traces of their presence by little transverse grooves and ridges upon the nails. The anterior part of the bed of the nail yields a thin layer of loosely-connected epidermic cells, upon which the body of the nail glides forward as upon a cushion; it may be assumed as highly probable that these cells likewise contribute, though in trifling measure, to the growth of the nail in thickness; this is rendered likely by the close adhesion of the nail to its bed; but it is far from being proved, and is even totally denied by *Henle*.

Now if the matrix of the nail become hyperplastic, the anterior part of its bed furnishes layer upon layer of these loosely-connected epidermic cells; the layers accumulate one upon the other, they raise the nail from its bed, and compel it to assume a more or less upright position; the hinder part of its bed, on the other hand, produces a thick and shapeless claw, several inches in length, spirally twisted, and somewhat incurved at its edges. Both of these conditions, which are so intimately related, may occur together; more usually, however, only one of them is present.

§ 307. WARTS may be broadly defined as hyperplastic overgrowths of the epidermis, in which the papillary body shares more or less; we will begin therefore with a few introductory observations on the mode of growth of the papillary body. It has already been stated that the very same cells which, after their migration from the connective tissue, are converted into epidermic cells by contact with the unaltered cuticle, are equally capable, before their migration, of serving for the development of connective tissue. The details of the process are well shown in a fine section through the apex of a rapidly-growing papilla of the skin (fig. 116). The boundary-line between connective tissue and epithelium appears very distinct at the sides of the papilla, where the small yellowish cells of the rete Malpighii are implanted in the fibrous texture of the papillary body, as described in treatises on normal histology. As we approach the apex of the papilla, this boundary-line fades and disappears; for on the one hand, the rounded cells of the connective tissue accumulate at the expense of the intercellular substance, while, on the other, the epithelial elements pass by slow gradations from these rounded forms, through a more

Fig. 116.



A hyperplastic papilla of the cutis with its epithelium. From the neighbourhood of an epithelioma of the lip.

spindle-shaped variety, till they finally assume the shape of ordinary pavement-cells. Thus the summit of the growing papilla is made up of embryonic cells passing externally into epithelium, and internally into connective tissue—a sort of "cambium" layer, such as exists in the stem of a plant between the bark and the wood.

§ 308. The COMMON HARD WART (*Verruca*) consists of a circular group of elongated papillæ, with their free extremities slightly enlarged and bulbous, their vessels dilated and extending close up to the epidermic covering. The latter, in marked contrast to ichthyosis, presents its normal threefold division, inasmuch as a thick layer of transition-cells fills up all the interstices between the enlarged papillæ, while the horny lamina invests the entire group with a common covering. At a later stage, when the wart attains an elevation of one line above the surrounding surface, the horny lamina exhibits rents and fissures which correspond to the interstices between the enlarged papillæ, and which gradually penetrate to the base of the wart. We are then able to see, without the aid of a lens, how many papillæ go to make up the wart. Their number varies from three to twenty and more; the size of the wart varies accordingly, from that of a pin's-head to that of a split bean. It seems, moreover, as though this dismemberment of the wart were the first step towards its spontaneous cure; the admission of air into its interior making the soft cells which it contains dry up together with the papillæ.

From an etiological point of view it may be interesting to know that the circular limit of the hyperplastic spot of skin corresponds to the area of distribution of a vessel of variable size. I can assert from personal observation that the very small, flat, discrete warts to which *Ascherson* has given the name of "Verrucæ planæ," and which are usually met with on the face and hands of adults, are often grouped in a manner suggestive of the ramifications of a vessel.

§ 309. The CAULIFLOWER EXCRESCENCES or papillomata of the skin, the smaller varieties of which are known as "Porrum" or "Acrothymion," differ from ordinary warts in that their constituent papillæ are destitute of a common covering; they are isolated from the first, each papilla growing in some measure independently. Their mode of growth resembles, upon the whole, that of ordinary warts; but in addition to the terminal, there is also a lateral apposition of young connective tissue, a dilatation and elongation of the capillary loops. An arborescent stroma of connective tissue is thus produced, whose outlines are repeated on a larger scale by the epidermic stratum.

§ 310. The smaller papillomata, such as the porrum, are very closely related, at any rate in outward form, to the POINTED CONDYLOMATA. These too are destitute of a common covering for the thickly-set, hyperplastic papillæ of the skin. They grow in just the same way, save that, as *Biesiadecki* has shown, a histological factor, which is of secondary importance in the normal growth of epithelium, takes a more prominent part in the development of acuminated condylomata. I allude to a certain fission of the epithelial cells, which is exclusively observed in the middle stratum of the epidermis—where cornification has not yet begun. The effect of this secondary growth of epithelium is barely appreciable in the normal development of the epidermis; to it we may ascribe the peculiar swelling of the epithelial border (fig. 39, *e*) which occurs during the skinning-over of granulating wounds; but it contributes most effectually to increase the thickness of the epithelial protrusions in epithelial cancer; in the pointed condylomata the extreme softness of the epidermic covering arrests attention, and this is due to the excessive development of the mucous layer. The red and fleshy aspect of the sycomata, which impart a sensation almost like that of mucous membrane to the finger, is also due to the fact that there is no thick horny layer to mask the colour and consistency of the young and vascular connective tissue.

FLAT CONDYLOMATA (*Condylomata lata*, *Plaques muqueuses*), must be sharply distinguished, in a histological point of view, from the pointed variety. The overgrowth of the papillary body is more diffuse; it is not confined to the tips of the papillæ, as in the papillomata just described. The overgrowth of the connective tissue predominates over that of the epidermis. Flat, rounded elevations about one line in height and from two to five lines in breadth, are thus produced; upon their surface the papillæ form secondary prominences. The colour of these condylomata varies from a pale to a dirty red; their epithelial layer is exceedingly thin; it is only in the folds between the adjacent prominences that a sort of cheesy epithelial substance accumulates, which undergoes further chemical changes and so gives rise to a most offensive smell. A catarrhal secretion of cells often takes place from the upper surface of the growth; sometimes too, the suppurative process extends deeper into the connective tissue.

§ 311. In the SOFT OR FLESHY WARTS (*Verruca carnosa, mollis*) the connective-tissue element of the growth preponderates to such an extent over the epithelial one, that most writers only refer to the epithelium because it not unfrequently presents a deeper pigmentation than usual of the rete Malpighii.

Many of the soft warts are congenital and are known as "Mothers' marks" (Nævi materni); others originate in advanced life, chiefly on the face and trunk. "The skin exhibits in these cases very gradual elevations, whose surface is usually flat, sometimes irregular, tuberculated or even warty. The epidermis and rete Malpighii, which extend over the growth, are seldom much altered; the cuticular investment is sometimes thicker than usual; but it never attains the same thickness as in the hard warts. If the growth be cut into, we see the cuticle spread over it in a uniform, rarely undulating layer. The growth itself is mainly situated in the cutis. It usually implicates the true papillary body and a certain part of the dermal tissue; in rare instances it involves the entire thickness of the cutis, or may even penetrate into the subcutaneous areolar tissue. In every case however, it contrasts markedly with the tougher and whiter tissue of the cutis, inasmuch as its texture is more transparent, of a bright grey or yellowish hue, often reddish-grey, more soft and juicy, occasionally gelatinous; not unfrequently too it is more coarsely vascularised. On investigating its structure, it is usually found to be very rich in cells, often indeed, it is all but entirely made up of relatively small cells with but little intercellular substance, and that little of soft consistency."

The above description of the soft wart is borrowed from *Virchow;* he goes on to direct attention to the histological identity of the tissue in question with granulation—(embryonic)—tissue, using this as a basis on which to build his explanation of the intimate connexion between soft warts and cutaneous sarcomata (*see* below).

§ 312. Let us linger a moment over the pigmented fleshy warts. *Virchow* has taught us to distinguish broadly between four varieties of abnormal pigmentation in the skin; these are—

1. Simple pigmentation of the rete Malpighii without marked changes in the cutis (freckles, &c.).
2. Pigmentation of the cutis without marked changes in the rete Malpighii and the epidermis.
3. Pigmentation of the rete where it invests a colourless overgrowth of the papillary body.
4. Pigmentation of the rete associated with a simultaneous deposit of pigment in a hyperplastic cutis.

The three last categories include all varieties of the pigmented mole; the two last are included in the pigmented warts. The pigment is deposited in the form of yellow, brown, or black granules, partly *in* the cells of the rete Malpighii and connective tissue, partly *outside* them, freely distributed throughout the connective tissue of the papillary body. It sometimes accumulates in such quantities as entirely to mask all peculiarities of structure; nothing but pigment-granules being visible. These form long striæ in the substance of the cutis, accompanying the larger afferent and efferent vessels.

It is very unusual to find, besides the pigmentation of the rete Malpighii, the nuclei of the older epidermic cells of a uniform black colour; indeed the nuclei, even of pigmented cells, are generally free from colouring-matter. I have observed this phenomenon on one occasion only; but I have failed to find any reference to it in books.

γ. *Heteroplastic Growths.*

§ 313. Two of the most important heteroplastic growths which affect the skin originate in the papillary body, or in the epidermis and papillary body together, while the remainder have their seat in the corium proper. The growths in question are epithelial cancer and sarcoma.

Epithelioma of the skin is very common; hence we took it as our type of the disease, in § 164. Here therefore I will confine myself to the discussion of a few points, which were passed over on that occasion. And first a few words concerning the local etiology of the growth.

Epithelioma of the skin occurs by preference at the junction of the skin with a mucous membrane; *sc.* on the lips, prepuce, anus, and vulva. When it occurs elsewhere, it is usually secondary, *i.e.* it is developed in parts which have been affected for years with some sort of morbid growth, without however exhibiting any of the characters of cancer. Among these are—

1. Some of the above-described overgrowths of the epidermis and papillary body, those more especially, which exhibit from the first a certain preponderance of the epidermic element, *sc.* cutaneous horns, hard warts, papillomata; this gives the classification we adopted in § 300 a very serious clinical significance.
2. Hypertrophy and dilatation of hair-sacs and sebaceous glands; atheromatous cysts.
3. Cicatrices, especially of the scalp.

The transition to epithelial cancer, as already stated, is inaugurated by an advance of the epidermic boundary, and consequently of the epidermis itself, inwards, towards the connective tissue—an advance which gives the growth a destructive, rodent character.

§ 314. The following varieties of cutaneous epithelioma are based partly upon the locality, partly upon striking anatomical peculiarities of the growth.

a. WARTY EPITHELIOMA. One of the most interesting and frequent complications of the anatomical appearances described in § 165 *et seqq.* is that with papillary excrescences. The mode of transition from cauliflower vegetations to epithelial cancer has already been described (§ 148). Closely connected with this is the circumstance that at the growing border of an epithelioma, in the zone where the sebaceous glands begin to be enlarged, warts, and even small cauliflower excrescences are not seldom found; and in this way the boundary-line between epithelium and connective tissue is displaced outwards, inverting the order of that displacement inwards, which occurs at the same time. Moreover papillary excrescences are often produced upon and within the epithelioma itself, the epithelioma being primary and the excrescence secondary. I need hardly say that in the production of these papillæ the stroma takes a leading part. It would seem however as though the release of the stroma, which follows the degeneration, softening and expulsion of the tap-shaped epithelial protrusions, contributed to change the direction in which the development of the epithelioma takes place. It is certain indeed, that the capillaries are peculiarly dilated in the softened parts, and project towards the cavities corresponding to the old epithelial protrusions, forming a number of closely aggregated loops. The secondary papillæ do not, as a rule, attain any great size; on the other hand they are very numerous, spreading uniformly over the whole of the ulcerated surface, or covering a great part of it in patches, like sedge upon a moor. So far as I know, no cauliflower growth of large size has ever been met with upon the surface of a cancroid ulcer.

b. CICATRISING EPITHELIOMA. This variety also is based upon a peculiarity in the behaviour of the stroma—and that after it has undergone infiltration. The skin of the face in old people is occasionally the seat of a form of epithelioma in which the infiltration never assumes any considerable proportions; it leaves no real ulceration in its train, but only a smooth scar. As its extension is exclusively horizontal, and proceeds from a single centre at a more or less uniform rate, it reminds us of a patch of lichen on a tree; hence its popular name of "rodent lichen" (Fressende Flechte). The point of histological interest about it, to which also it owes its general aspect, is that the residual stroma, which usually produces pus or papillæ, is directly converted into a stiff cicatricial tissue, with a great tendency to contract; this remains coated with a thin layer of epithelium.

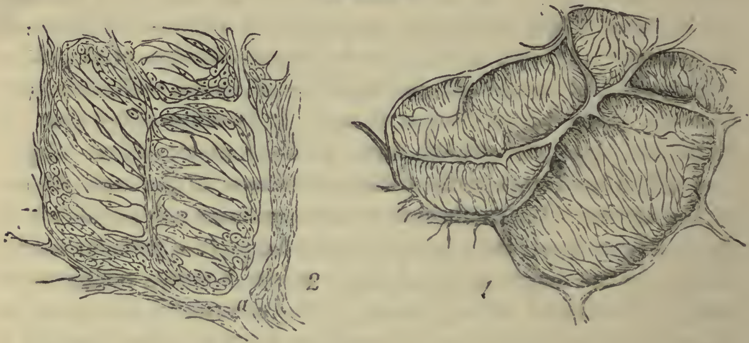
§ 315. SARCOMA of the skin exhibits certain peculiarities in the mode of its development, which necessitate a comparison of it with cutaneous epithelioma. Not the least important of the services which *Virchow* has rendered to the subject of the sarcomata, is his demonstration of the fact that cutaneous sarcomata very frequently originate at such points as are predisposed thereto by other anatomical conditions. Among such local causes, the soft, fleshy wart occupies as prominent a place, as the hard wart, cauliflower excrescence, porrum, and cutaneous horn do with reference to epithelioma. Those hyperplastic conditions of the cutaneous surface therefore, in which the connective tissue predominates, always threaten to pass into sarcomata. Foremost among these are the soft, pigmented warts (*nævus pigmentatus*); this disastrous tendency has long been known. They give rise, not to white, but to pigmented sarcomata, so that the local predisposition extends its influence even to a collateral circumstance like this. Tumours which spring from soft warts usually continue to betray their origin for a long period, even in their broader outlines—presenting themselves in the form of true "fungi," *i.e.* true mushroom-like proliferations, with a broad base and overhanging edges. But even in tumours of large size, their origin from the papillary body may soon be established by minute examination also. The cutis proper extends unaltered beneath the tumour; and this even where it is displaced and dragged into the pedicle.

Again, scars predispose to the development of sarcomata. The sarcoma of scars is also known as "false keloid." By the term KELOID, *Alibert* denotes a scar-like tumour of the skin. It forms oval protuberances of a red colour and tough consistency, often with claw-like prolongations; its surface is smooth, and it is usually found in parts of the skin which were previously healthy. The tissue may be termed sarcomatous, and the arborescent distribution of the growth is ascribed by *Collins Warren* (Sitzb. d. K. Akadem. d. Wissensch. Bd. lvii., 1868) to its localisation round the smaller arteries of the cutis. It is otherwise with the FALSE KELOID. This may be said rather to replace a scar than to grow out of one. In the regular course of the development of a scar, the presence of round-cell and spindle-cell tissue is only provisional; they speedily give place to fibroid tissue. Now if either the one or the other element persists longer than its proper time, and if it accumulates in disproportionate amount, we get, instead of a scar, a tumour belonging to the sarcomatous series. Even fungous granulations (§ 105) may be viewed in this light; and they form one extreme of a series of transitional forms, whose other extreme is represented by the most luxuriant and malignant sarcomata.

In addition to the above, *Virchow* has directed attention to a local cause which determines the formation of many cutaneous sarcomata. Repeated irritation and inflammation is one of the most frequent and efficient excitants of sarcomatosis; another proof that our comparison of the sarcomata with the products of inflammatory proliferation rests on a deeper foundation than the mere form of the cells (*Virchow*, Krankh. Geschwülste, Bd. ii. p. 246, *seqq.*).

§ 316. Fibromata of the papillary body deserve especial notice. They differ from fibromata of other organs in their greater softness; hence they derive their name of "Molluscum." Fibroma Molluscum (*Virchow*) is usually multiple, so that we are able to study every stage of its development in a single case (cf. *Virchow*, Kr. Geschw. i., 325 and frontispiece). A small group of papillæ, perhaps even a single papilla (for this point is still *sub judicè*) furnishes the materials for a roundish nodule, which may pass through every gradation of size, from that of a millet-seed to that of a man's head and upwards. In its interior the various stages of growth succeed one another as follows: the younger nodules, and the more recent portions of the older ones, consist of round-cell and spindle-cell tissue, while the older ones are made up of fibrous tissue. It is noteworthy that in its fibrous stage, the growth never exhibits that extreme toughness which is characteristic of old cicatrices or of the *corps fibreux* of the uterus. The molluscum always remains soft; and this is due, as I can assert from personal knowledge, to a peculiar modification in the development of the connective tissue, owing to its being complicated with œdema. The connective tissue as it approaches maturity, does not contract from all sides towards a single centre, in the usual way, and so shrink together as a whole; it contracts round certain lines which traverse the mass, and which coincide in the main with the course taken by the vessels. We meet with this modification in the development of fibrous tissue wherever the islets of parenchyma undergo a metamorphosis requiring space for its completion; so *e.g.* it occurs in the development of clusters of fat-cells, in enchondromata, myxomata and colloid cancers. The connective tissue forming the stroma of these tumours represents the major part of the original basis of embryonic tissue, which, as the specific differentiation progresses, and the originally minor part undergoes a disproportionate increase in bulk, becomes converted into a narrow framework for the reception of the islets of cartilage, granules of colloid matter, clusters of fat-cells, &c. The present case is simply one of œdema, due probably to some disturbance of the circulation, and occurring in the molluscum-nodule at an early period. The fluid requires space. Hence even in that early stage, when the mass consists of round-cells, elongated fissures make their appearance in the parenchymatous islets of the tumour (fig. 117). These fissures, which contain the dropsical fluid, increase in size; soon we come to speak of bands of connective tissue stretched between the vessels; and when the fibroid development is complete, the entire mass is represented by a network of thick trabeculæ of connective tissue, whose meshes are bridged over by thinner fasciculi of fibres (fig. 117). It is self-evident that this structure must be quite as soft, nay, softer than ordinary granulation-tissue. If therefore the word "molluscum" be derived from "mollis" (and this hardly admits of doubt), no fitter name could possibly be found; inasmuch as softness is, throughout the entire life of these tumours, their chief characteristic.

Fig. 117.



Fibroma molluscum. 1. Mature (after *Virchow*); 2. Immature. Formation of clefts in the islets of parenchyma. $\frac{1}{200}$. At *a*. the lumen of a vessel.

2. Diseases of the Corium and Subcutaneous Areolar Tissue.

§ 317. The position of the corium in pathological histology is actually determined by the important circumstance that it constitutes the greatest continuous accumulation of vascular connective tissue in the body. *A priori* therefore, we should expect to meet, not so much with a series of novel and peculiar appearances, as with a very clear, I might almost say, typical evolution of the familiar histological potentialities of the intermediate apparatus of nutrition. Nor are we doomed to disappointment. With the exception of miliary tubercle and enchondroma, there is hardly any product of the conjoint vascular and connective-tissue system which does not attain to its fullest perfection in the corium; some of these, particularly the specific products of leprosy, glanders, and syphilis, even exhibit a marked predilection for the skin. Lupus is exclusively confined to the skin; but recent observations compel me to regard this as a growth which originates in the sebaceous and sudoriparous glands, and therefore to refuse it that place among the diseases of the corium to which most authorities consider it entitled.

a. *Inflammation.*

§ 318. The corium proper, according to a very noteworthy investigation by *Rollett*, is built up of thick bundles of fibres (of connective tissue) which traverse it obliquely, starting from the subcutaneous areolar tissue; these break up as they advance towards the surface, and interweave with neighbouring fibres to form a web of extraordinary density. Moreover, the individual fibrillæ are of exceeding toughness, offering an obstinate resistance to softening and liquefaction. Owing therefore to the closeness of texture, as well as the toughness of its constituent fibres, the corium proper is little suited for the exhibition of such processes as claim much space in short periods of time, and in particular, of suppurative inflammations. When we come to consider those inflammations which start from the hair-sacs—acne and furunculi—we shall see how cumbersome an attitude is taken up by the corium towards each acute inflammation in turn. The behaviour of the subcutaneous areolar tissue is very different. It offers no obstacle to the spread of suppuration. The fibres of the areolar connective tissue are soft and readily dissolved; between them are meshes and lacunæ (the "cells" of the "cellular" tissue) smooth internally, and occupied by fluid or clusters of fat-cells. In these meshes, around the fatty clusters, there is enough space to accommodate three times the amount of fluid which is usually present. Add to this that here, between the muscles and the skin, an extremely free communication between neighbouring parts is kept up by the lymphatics and blood-vessels; in short, every facility is afforded for the extension of a subcutaneous suppurative process.

We must keep these facts continually before our eyes in studying the *acute* inflammations of the skin. They shed a flood of light upon the course of phlegmonous abscesses, when the corium shows only too well its capacity for hindering the escape of the pus accumulated underneath it. No important novelty is contributed to pathological histology by the study of this form of inflammation. It simply exhibits suppuration and abscess-formation in its most typical form—and on the largest scale—such as has been described already in the General Part of this work (§ 94, *et seqq.*).

The most exquisite example we possess of CHRONIC inflammation affecting the skin, is afforded by the so-called *Sclerodermia adultorum* (not to be confused with *sclerema neonatorum* or with *elephantiasis*). *Rasmussen* makes an infiltration of the perivascular sheaths with small cells the starting-point of the textural alterations (*Hospital-Tidende*, 1867). Extending farther, this leads to a more diffuse production of young connective tissue, which subsequently contracts and causes a peculiar puckering of the cutaneous surface. The skin grows smooth and shiny, and is very closely applied to underlying parts, *e.g.* to the condyles of the humerus in the neighbourhood of the elbow-joint; distortions and deformities arise in consequence, just as if the affected regions of the skin were cicatrices. We shall meet with precisely analogous conditions in the liver and the kidneys, where they receive the name of cirrhosis and granular atrophy.

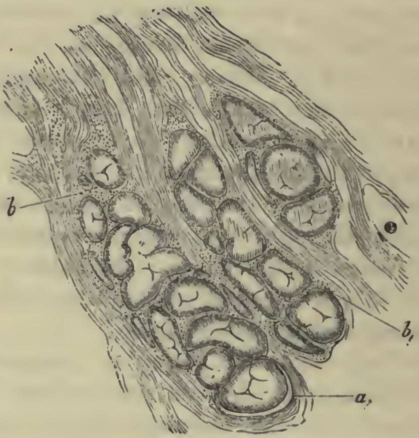
β. *Hypertrophy.*

§ 319. One of the most peculiar and interesting of all the diseases to which the skin is liable, ELEPHANTIASIS ARABUM, must be regarded as a hypertrophy of the corium and subcutaneous connective tissue. It owes its name to the striking resemblance between the lower extremity of a man affected with this disease, and that of an elephant. The skin, prodigiously thickened, hangs in wide baggy folds about the leg and ankle, so that the toes can barely be detected peeping out from under them. On section, we recognise the familiar structure of the cutis, only on a larger scale. As regards its etiology, I will only remark at present, that we have many reasons for believing it to be a chronic inflammation. Our description of *eczema rubrum* on a former page, was broken off abruptly at the point where it passed into chronic inflammatory thickening of the cutis. We reserved this for our chapter on Elephantiasis, because no anatomical difference of any moment can be shown to exist between these two forms of cutaneous hypertrophy. Moreover in those countries where elephantiasis is endemic (the tropical and subtropical regions of the globe), it is a well-known fact that the disorder usually begins with phenomena having all the characters of erysipelas (see § 288). During this inflammatory stage the lymphatic glands, which receive their lymph immediately from the inflamed part, become swollen ; in erysipelas of the leg, the inguinal glands, in that of the arm the axillary, in that of the face the cervical glands. The swollen glands do not subside. The lymph-paths through them remain permanently blocked. There ensues a stasis of the lymph ; the outflow of the superfluous nutrient fluid is checked, and this must be regarded as the immediate cause of the hypertrophy.

§ 320. We will begin by giving a general sketch of the histology of elephantiasis, derived from recent investigations. *Teichmann* asserts that the above-described dilatation of the lymphatics may be traced to their origin in the papillæ of the skin. *Virchow* adds that an irritative condition of the corpuscular elements of the connective tissue may be shown to exist from the very first, in parts affected with elephantiasis ; proliferation of nuclei and fissiparous multiplication of cells being found particularly in the radicles of the lymphatics. The smallest lymph-paths are richly lined with an epithelial stratum of unusual thickness. This would point to a direct connexion between the morbid growth and its chief causal element, the dilatation of the lymphatics.

I regret that I cannot speak of the first beginnings of elephantiasis from personal observation. I have only had the opportunity of subjecting its later stages to an adequate histological analysis. Here too, the blood-vessels and lymphatics play a prominent part ; but what chiefly arrests attention is the increased bulk and simultaneous condensation of the existing bundles of connective tissue. How, we may inquire, is this brought about? The cutis is a web of fasciculi of connective tissue. In transverse sections these fasciculi are divided, some transversely, some longitudinally, others at every imaginable angle. Now if we select a point at which a bundle of longitudinal fibres happens to abut upon a bundle which has been divided at right angles or obliquely (fig. 118), we find that the longitudinal fibres separate to include those which are divided transversely.

FIG. 118.



Elephantiasis. Connective-tissue bundles of the cutis seen in longitudinal and transverse section. *a.* Lymphatic spaces surrounding transversely-divided bundles; *b.* Protoplasm, at whose expense the bundles increase in length and thickness. $\frac{1}{500}$.

They form a framework whose trabeculæ are ingeniously interwoven with the fibres of the bundle which is cut across. This framework however is of a much softer and more delicate consistency than the main fibres. It refracts light less highly, and is not so susceptible of being stained by carmine. Of course the transition from the one variety to the other is extremely gradual. In other words, the fasciculi of connective tissue in the skin affected by elephantiasis, divide at each end into a number of finer and softer fibres, which make up a framework for the reception of the central portions of other bundles, whose position in relation to the first set, is transverse or oblique. Repeated examination failed to show any traces of embryonic tissue. If I am called upon to express an opinion as to the mode in which the cutaneous connective tissue increases in amount during the later stages of elephantiasis, I cannot deny the probability that the elongation of the fibrillæ is primarily due to the progressive and gradual hardening of the soft material at their ends. This view indeed rests chiefly upon the absence of any other productive process in the hyperplastic cutis; it affords a very plausible explanation, however, of the naked-eye appearances.

The fibres at first grow thicker at the expense of the same material to which their elongation is due. This seems at first sight paradoxical. But we must recollect that the soft ends of the fibres are at the same time the cement for the agglutination of such bundles as run in other directions. Why cannot the same material serve for the elongation of some fibres while it contributes to the increase in thickness of others? The latter increase however has its limits. No sooner does the fibre attain an average diameter of half a millimetre than it separates sharply from the cement round it; a true interstice is thus produced, which isolates the fibre completely for a variable part of its extent. These interstices undoubtedly communicate with the lymphatic system, and contain those large quantities of clear, coagulable lymph, which flow from the recently divided surface of the affected skin. They attain their highest development at the junction of the cutis with the subcutaneous connective tissue. Here too we find the thickest of the fibrous bundles. Higher up, in the outer portions of the cutis, the fibres are thinner; no vestige of interfibrillar spaces can be seen, nor any of dilated lymphatics, such as one might expect to find, in accordance with the observations of *Virchow* and *Teichmann* on the early stages of the process. The state of the capillaries is much more striking. The capillary network of the cutis is neither closer nor more abundant than usual; on the contrary, it is obviously nothing more than the old capillary network stretched over a greater area; the individual vessels however are wide and gaping; their walls are intimately fused with the surrounding connective tissue. The lumina of the vessels in the dense substance of the cutis, closely resemble the channels excavated in worm-eaten wood. I am inclined to call this the first stage of cavernous metamorphosis, reminding the reader that *Hecker* has described a case of congenital elephantiasis in which the tissue distinctly exhibited a cavernous structure. This condition of the vessels however, occurs in all fibromata; and for the conversion of an ordinary fibroma into a cavernous fibroma, a peculiar process of contraction has first to take place along the axes of the vessels (cf. § 129).

The elephantiastic overgrowth spreads from the cutis into the subcutaneous areolar tissue; first the fasciæ, finally the intermuscular and periosteal connective tissue, become involved. The more complex organs, such as muscles and nerves, which are included in the growth, as well as the adipose tissue, undergo atrophy and disappear. The periosteal growth leads to enlargement of the bones by the apposition of new layers of osseous substance. Numberless exostoses cover their surface; affording ample proof of the possibility of true bone being developed, not from the periosteum only, but from the adjacent intermuscular connective tissue as well. On the other hand the papillary body is involved in the hypertrophy. The papillary body is, after all, only the outermost layer of the cutis. The skin in elephantiasis is therefore very often covered with overgrown papillæ, and also with thorny projections, which make it look like an ox's tongue. The process, however, is always more widely spread in the deeper layers of the cutis, than in the papillary body; the implication of the latter being always secondary.

§ 321. Pachydermia lymphangiectatica, an interesting variety of ordinary elephantiasis, has its seat of election in the scrotum, penis, mons veneris, and the anterior part of the perinæum. The hypertrophied skin is studded with innumerable vesicles, the largest of which is not bigger than a pea; it is evident at the first glance, that these vesicles are not produced by detachment of the cuticle, as in the bullous exanthem, but that they are really cavities in the uppermost layer of the cutis itself. For their roof is comparatively tough; the clear fluid they contain, can be squeezed out of them, returning in proportion as the pressure remits. On puncturing any one vesicle, true lymph flows from the puncture, often in enormous quantities, while the swollen cutis and all the other vesicles subside contemporaneously. This shows clearly enough that the vesicles are in connection with the lymphatic system; but the histological investigation of vertical sections through the affected skin, affords additional evidence that it is the superficial, sub-papillary network of lymphatic vessels, which has undergone partial ampulliform dilatation. The vesicles are roofed in by the epidermis together with the papillary body. As a rule, the detached portion of the papillary body contains from four to six papillæ; in the smaller vesicles, these are still tolerably long and slender; in the larger ones, they assume a broader and shorter form; I have never seen them stretched to such a degree as no longer to be recognisable. All the vesicles are lined with the well-known mosaic of endothelial cells; and this places their origin from dilated lymphatics beyond all doubt. We have still to find out the special cause of the peculiar modification of the anatomical appearances. I feel myself obliged to look for it in the implication of the unstriped muscular fibres of the skin in the hyperplastic process. We know that the tract of skin which is peculiarly liable to be affected by pachydermia lymphangiectatica is also very richly endowed with involuntary muscular fibres; indeed the tunica dartos of the scrotum is an independent muscular membrane (cf. *Neumann* on the Distribution of the Fibres of Organic Muscle, in Wiener Sitzb. 1868, p. 651). Now in the case which I had an opportunity of examining, and which presented the anatomical features of the disease in their most typical form, there was a very distinct overgrowth and proliferation of unstriped muscular fibres; they were grouped in well-marked, compact fasciculi, which permeated the entire thickness of the corium—radiating obliquely from below upwards in all imaginable directions. The corium indeed, was made up of muscular and fibrous elements in nearly equal proportions. Setting aside the likelihood of compression of the lymphatic trunks by the actual contractions of this exuberant muscular layer (of those trunks which, passing vertically through the cutis, serve to connect the superficial with the deeper network of lymphatic vessels), and the consequent ampullary dilatation of the superficial network; it cannot be denied that a somewhat similar effect would needs be produced by the mere elastic reaction of the muscular parenchyma, when this is developed, as in the present case, in a region singularly incapable of yielding to the demands of new products, of whatever kind, for more space. Hence I am led to believe that the overgrowth of the muscular fibres is to be regarded as the chief cause of the lymphangiectasis, by hindering the circulation of the lymph in the substance of the corium proper.

γ. *Heteroplastic Growths.*

§ 322. A reference to the discussions embodied in the General Part of the present treatise will allow us to be very brief in speaking of those heteroplastic growths to which the skin is liable. This applies more particularly to myxomatous and lipomatous tumours, which originate by preference in the subcutaneous areolar tissue; also to cavernous growths, to the sarcomata and fibroid tumours, which may occasionally be met with in the subcutaneous tissue.

The various kinds of CARCINOMA usually affect the skin only in a secondary manner; for we either find a cancer of deeper parts, *e.g.* of a lymphatic gland, a muscle, or a bone, making its way outwards to the skin by continuity of tissue, or else a true metastatic deposit in the skin, formed during the later stages of carcinomatosis. In the latter case, the disease usually assumes the form of flattened tubera varying in size from a pea to a hazel-nut, mainly confined to the skin of the trunk. The name of "ivory cancer of the skin" (*Alibert*), or "cancer en cuirasse" (*Cruveilhier*), is applied to a scirrhous or colloid cancer of the mammary gland, when this extends in small but closely aggregated nodules over the entire skin of the front of the chest, converting it into a tough, white, translucent, smooth, and lustrous rind, as hard as a board.

§ 323. The specific products of leprosy, of syphilis, and (supposing my own view to be wrong)* of lupus, form, in respect of their histology, a natural group, which, as we have already had occasion to see, is distinguished by its peculiar hybrid position on the border-land between inflammation and tumours. The acme of the tissue-development, the point at which it culminates, is the production of an embryonic tissue, which so closely resembles the familiar inflammatory proliferation of connective tissue, that *Virchow* has actually given it the name of granulation-tissue, and has embodied the whole in a class of "granulation-growths" (Granulationsgewächse). Notwithstanding this, no one would dream of simply including them among the products of inflammation; at the very least, they would be called "specific" inflammations. Their specific character does not however reside exclusively in their etiological relations; it is also based on demonstrable anatomical peculiarities. The very way in which the embryonic tissue is brought together deserves special notice. It takes the form of nodular (tuberous) deposits in the connective tissue of the cutis. The individual nodules attain the size of a pea, or even that of a cherry or more. This would of itself be a phenomenon of extreme rarity in the history of simple inflammatory growth; it would rather deserve to be termed "sarcomatous." Still more important is *the way in which the growth lingers on the confines between organisation and decay.* By slow gradations—it would seem—the embryonic tissue passes, either into connective tissue, or into pus; or its cells become fatty while its intercellular substance undergoes mucous softening. We get a series of very characteristic intermediate forms, of which we appreciate the value when we attempt to distinguish between the individual members of the group.

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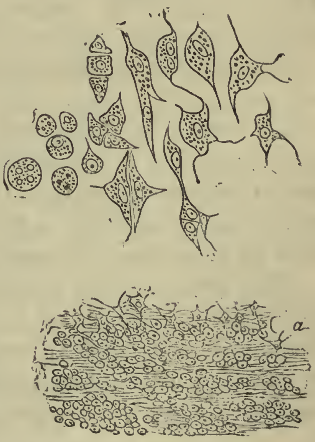
* Cf. § 317, last sentence.

§ 324. THE SYPHILITIC GUMMA has been fully described elsewhere. The chief anatomical criterion of its specific character was found to reside in the partial fatty degeneration of the granulation-tissue, in the production of cheesy centres amid a continuous accumulation of newly-formed connective tissue. The gummatous deposit in the skin deviates from this type in the greater rapidity of its course, and in several other points also. Gummata of the skin are rarely single; they are usually multiple, arranged in groups which occupy a certain tract of the cutaneous surface (*Lupus syphiliticus*). The nodules are seated in the parenchyma of the cutis, and even when they cause no visible projection, they may be detected all the more readily by the finger. The peculiar hardness which characterises them at first, speedily passes, as a rule, into the opposite extreme. The tendency of the cutaneous gumma to undergo softening, is well known. This end is reached by the co-operation of suppuration with fatty degeneration; in this case, as in many others, they form links in one chain, suppuration freeing the cells from their organic connexion, while fatty degeneration indicates the immediate result of this isolation—*sc.* their atrophy and death. The focus of softening then gives way, and liberates its contents: a circumscribed loss of substance being left. Its floor and walls are infiltrated to the extent of a line and more with young cells; this gives a dash of white to their colour, and makes them tough and bacony. A thin fluid containing a few cells and some fatty *débris*, exudes from the raw surface; the adjacent bundles of connective tissue are slowly dissolved, and the ulcer continues to increase in size until its further progress is arrested by vigorous anti-syphilitic treatment. Then, and not before, a permanent layer of embryonic tissue is formed upon the floor of the ulcer; it is then, and not before, that the formation of a scar begins. Syphilitic scars have a strong tendency to contract. Causing the utmost distortion of neighbouring parts, they shrink themselves to a mere nothing, so that after the lapse of a certain time it is often impossible to infer the previous existence of a syphilitic ulcer from the presence of a scar. This peculiarity too, has not been explained as yet by the results of microscopic investigation. A syphilitic scar resembles all other scars both in its structure and development. The blood-vessels are invariably obliterated; in injected specimens the syphilitic scar looks like a gap in the vascular network of the skin; whether the powerful contraction of the connective tissue may not be the cause of this total obliteration of the vessels, must remain an open question.

So much for the development of a single syphilitic tubercle in the skin. The growth and decay of many such aggregated nodules lies at the root of syphilitic lupus. The nodules are now small and superficial, now deeply seated and large. In the former case they are usually grouped concentrically round the point which was first affected; discoidal ulcers result which become annular by healing from the centre, where a cicatrix is formed (*Lupus syphiliticus serpiginosus*). In the latter case the ulcers grow deeper, they extend into the areolar tissue (*Lupus syph. exulcerans*). There is also a hypertrophic variety of syphilitic lupus, in which isolated nodules of relatively small size are developed in an abundant matrix of newly-formed connective tissue.

§ 325. The pathological anatomy of LEPROSY was shrouded in darkness till a very recent period. It was in 1848 that *Danielssen* and *Boeck's* work on the Norwegian *Spedalsked* appeared in Paris, a work illustrated with admirable drawings. Since then *Virchow* has taken the matter in hand, and has subjected it to a most exhaustive treatment in his work on Tumours. All the affections observed in the course of leprosy are based, histologically speaking, on a common foundation. This is a change in the connective tissue which leads, in the skin, to the formation of the well-known leprous tubercles. After a prolonged initiatory stage, during which the skin is reddened in patches and exhibits bossy swellings, a number of nodules are developed in the substance of the cutis or in the subcutaneous tissue; these vary in size from a hazel-nut to a walnut; they are hard, and more or less prominent according to their situation. They give the skin a tuberculated aspect; occurring by preference upon the face and hands, they lead to the most repulsive deformities. Microscopical analysis in the hands of *Virchow* yielded invariably the same results. The nodules consisted throughout of granulation-tissue, very rich in cells. This tissue extended from the rete Malpighii to the subcutaneous layer of adipose tissue; it surrounded the hair-sacs and sebaceous glands, causing their atrophy by disturbing their nutrition. Hence it is that the tubercles of leprosy, even when seated on the hairy scalp, are always hairless. The accompanying woodcut is copied from fig. 178 in *Virchow's* book on Tumours, and shows the leprous tissue under a considerable magnifying power. *Virchow* adds that he has nowhere traced the progressive development of a simple spindle-shaped or stellate connective-tissue corpuscle through all the stages of nuclear and corpuscular proliferation so perfectly as here. The cells divide; they grow smaller and more numerous; the intercellular substance is represented by very narrow bands of a material which is rendered granular and cloudy by acetic acid, and which

FIG. 119.



Tissue of leprous tubercles (after *Virchow*). Cells undergoing division.

must therefore contain mucin. The ultimate result of these changes is the texture represented in fig. 119, *a*, which may be regarded as embryonic tissue of the most typical kind.* So far therefore, the leprous nodule, though distinguished from the syphilitic product by its size and its occurrence in a multiple form, agrees with it most absolutely in being composed of granulation-tissue. The agreement is absolute in this respect until retrograde metamorphosis sets in. The leprous product indeed, like that of syphilis, undergoes disintegration by a combined process of fatty degeneration and suppuration ; it differs from it in the long period of its precarious quiescence. For we may fairly term the condition of a tissue precarious, when it contains a vast number of elementary parts requiring nourishment, parts which have taken the place of a parenchyma at once smaller in bulk and containing fewer cells ; and this without any adequate increase in the supply of nutrient material by a simultaneous formation of new vessels. Retrograde metamorphosis or suppuration might be expected to set in at once. But neither of these changes seems in any hurry to begin. At last, after years have elapsed, the nodule becomes softer, its intercellular substance undergoes partial liquefaction, some of the cells are destroyed by fatty change ; but complete resolution can only occur if the growth was very limited in extent. The nodule passes into suppuration and ulceration only if it is exposed in an exceptional degree to violence and other sources of external irritation. A slight increase of cell-growth then converts the leprous nodule into pus, which is evacuated externally, leaving a proportionate loss of substance behind it. The leprous ulcer thus produced continues to discharge a thin and sanious pus, which usually dries up into brownish crusts.

The same specific product of morbid growth underlies the other disorders incidental to leprosy. Thus *e.g.* the cutaneous anæsthesia is due to the growth of nodules upon the nerves ; the spontaneous disarticulations of the limbs are caused on the one hand by the gradual extension of the infiltration to deeper parts, on the other by a painless suppurative disorganisation of the joints which finally results in complete separation.

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* *Hansen* states (Nordiskt Medicidskt Arkiv. i., 13) that in the older leprous tubercles, cells are found which contain, besides a nucleus, a brownish oily spherule, together with peculiar amorphous bodies of large size which seem to be entirely made up of such spherules.

§ 326. Glanders, communicated from the horse to man, manifests itself also by the production of nodular deposits in the subcutaneous areolar tissue. The deposits are entirely made up of embryonic tissue, and differ from the corresponding products of syphilis and leprosy in a speedier rate of change, terminating invariably in suppuration.

3. Diseases of the Hair-Follicles and Sebaceous Glands.

a. *Retention of Secretions.*

§ 327. The hair-sac, with its appended sebaceous follicles, is one of the most ingenious anatomical contrivances in the body. The whole arrangement for the implantation of the hair into the skin, the ingenuity with which it is provided for in the interior of the hair-sac—all this agrees wonderfully with our notions of the adaptation of means to ends. But, as in the case of many an ingenious contrivance due to human skill, the advantages are not without corresponding drawbacks. Both are easily put out of order. The way in which the growing hair moves upwards along its sheath, at whose narrowest part it is brought in contact with the openings of the sebaceous glands, which oil it with their secretion, and protect it against the adverse influences with which it will have to contend upon its liberation—all this looks wonderfully cunning and practical. But the very closeness of this contact between the hair and the neck of the follicle has its dangers. It wants but little to stop up the mouth of the follicle completely. A trifling swelling of the subepidermic connective tissue, a slight increase in the number of epidermic cells produced, is quite enough to fill the small amount of vacant space which still exists in the neck of the sac. The excretory duct once plugged, the secretion cannot escape, and a whole series of disorders of the hair-sacs, due to retained secretions, are the result. These we will now proceed to describe.

§ 328. Pausing for a moment to consider the etiology of retention, we find that a closure of the hair-follicle by dirt from without, is comparatively rare. Any substance which could not be expelled and pushed aside by the vigorous advance of the growing hair, would have to be endowed with a very extraordinary degree both of penetrating power and viscosity. A far more important cause of retention is the over-secretion of epidermis and tumefaction of the subepidermic connective tissue about the mouth of the hair-sac, to which allusion has been made above. In one of the disorders which we shall have to consider, viz. acne, both of these phenomena are simultaneously produced by one and the same cause, *sc.* a subacute inflammatory state; and it seems fair to assume a like mode of causation in other cases which are complicated by inflammation. All these causes however, sink into insignificance in the face of a circumstance which throws the very question as to the mechanism and causes of occlusion into the remote background; I mean the circumstance that the structure of the hair-sac affords the most favourable opportunities for an accumulation of secreted matter, without any previous occlusion of the efferent duct.

The hair-sac (*see* fig. 109) is club-shaped in form; the diameter of its fundus exceeds that of its mouth; its walls face partially downwards; indeed that portion of the follicular wall which immediately surrounds the hair-root, may be decidedly said to be turned *away from* the surface of the skin. Hence the secretions from the wall of the follicle find their escape hindered by that wall itself. It is only the vigorous growth of the hair which prevents the cells shed by the epidermic lining of the follicle, from remaining in its interior. The hair drags them with it as it grows; the upward and outward direction of the little scales of its cuticle contributing to this result. The hair may be said to scour out the little recess in which it grows. But it is obvious that this self-cleansing apparatus is only adapted to cope with a very moderate amount of epidermic desquamation on the part of the follicular lining. The least increase of this must necessarily lead to the retention of the secreted matter. Accordingly the question as to what stops up the follicle becomes futile. We ought rather to inquire how it is that the secretions are not usually retained—considering the peculiar structure of the hair-sac. In my opinion, this is the point of view which we ought to take up, with reference to the etiology of retention in the hair-follicles, which is otherwise so enigmatical. The starting-point of the disorder consists in over-secretion from the follicular lining; and this serves also to explain the occurrence of retention. In the majority of instances the over-secretion in the hair-sacs is merely a part of a general disorder of the whole cutaneous surface, in which its recesses take part in their due measure. Persons whose skins are naturally greasy, whose hair and nails grow fast, whose heads are always full of scurf—young men at the time of puberty—are therefore specially predisposed to diseases caused by retention of secretions in the hair-sacs. Moreover we often find them in the neighbourhood of epitheliomata and warts—wherever indeed a proliferation of cuticular elements is an essential feature of the anatomical alterations.

§ 329. Granting therefore that we have to do with over-secretion in the interior of a hair-follicle, we next proceed to inquire whether this affects the follicle in its entirety or only a portion of it. The former is the case in COMEDO. This term is applied to a condition in which the entire length of the hair-sac is uniformly distended by an accumulation of epidermic products. The skin may easily be raised from its bed at this point. If we squeeze it firmly on each side of the comedo, a small whitish plug is driven out of the sac, which exhibits a black spot on its free end, and has accordingly been compared to a living organism—a maggot—(comedo). Of course, the appearance in question is due to the impregnation of the free end with dirt from without. If we put the plug in a drop of water and examine it microscopically, we find nothing beyond epidermic scales, which here and there exhibit an opaquely-dotted appearance due to the presence of oil-globules. Besides this we find free oil-globules, furnished by the sebaceous glands. According to *Gustav Simon* a very small six-legged parasite with a long abdomen, the *acarus folliculorum*, is more common in these than in normal hair-sacs. I have never seen it. Comedones are usually found on the alæ and bridge of the nose, and on the shoulders—wherever the skin is coated with down only. They do not affect the hair-follicles of the scalp and chin.

§ 330. If the over-secretion is restricted to the fundus of the sac, the resulting appearances are somewhat different. The epidermic masses form concentric laminæ round a central nucleus, consisting of a spheroidal aggregate of cells; an epidermic globe is thus produced, which differs from the "pearly nodule" of epithelioma only by its greater size. Should the globe attain the dimensions of a millet-seed, it communicates a yellowish-white tint to the overlying epidermis, and receives the name of MILIUM or GRUTUM.

§ 331. A third variety is the MELICERIS, so called from the honey-like character of the follicular contents; this is due to a more abundant admixture of oily matter from the sebaceous glands with the epidermic products. If the nodule project markedly above the surface, if the distended follicle protrude more and more above the level of the surrounding skin, and if the connective tissue of the papillary body take part in the hyperplastic process, the MOLLUSCUM CONTAGIOSUM results. This is a wart-like prominence as big as a pea, differing from other soft warts which resemble it, only in having its centre occupied by a dilated hair-sac which secretes fatty and epidermic products in abundance. The hypothesis of an antecedent occlusion of the hair-follicle is least of all—be it said in passing—applicable to molluscum contagiosum. In the larger molluscous tumours, the follicular orifice is often found gaping to such an extent that the contained matters may be squeezed out with the utmost ease. It has been asserted that these matters are capable of transferring the disease to the skin of a healthy person. The assertion rests on a very doubtful substratum of evidence; it has given rise however to the questionable epithet "contagiosum."

§ 332. The ACROCHORDON is a small cutaneous polypus, often with a very long pedicle. It looks as if a small, crooked, brown wart were hanging from the skin of the neck or trunk. On examining the head of this little tumour, we find in its interior one or two hair-follicles much distended with sebum, &c. We may reasonably assume that this retention gave rise to a warty projection, which subsequently became polypoid. The length of the pedicle, which is often very striking, is usually due to accidental causes—particularly to a bad habit of playing with and pulling at such tumours.

§ 333. We come finally to the ATHEROMATOUS CYST, the highest degree to which the simple retention of secreted matters in a hair-sac is capable of attaining. The follicle is distended by the accumulated secretions till it reaches the size of a pigeon's egg, or even a child's fist. It becomes a retention-cyst, in which we are able to distinguish between a secreting cyst-wall and secreted contents. The former is composed of a connective tissue rich in cells, lined by from two to three layers of pavement epithelium. Its thickness is in inverse proportion to the size of the tumour; it may ultimately become as thin as a serous membrane. Nevertheless we must always regard it as a hyperplastic product, inasmuch as the sac of connective tissue in which it originated, is the thinnest of all the layers and sheaths of the hair-follicle. This sac must therefore have undergone a striking increase, both in superficial area and in thickness; and although I am far from wishing to assert that this increase in size is the cause of the over-secretion and retention, it nevertheless seems to me a very important fact, that in proportion to the gradual increase in the production of epithelium, the area, not only of the epithelial layer itself, but that of the organ which I regard as the matrix of the epithelium, has also undergone an increase. Moreover it is clear that the increased production of epithelium is at once the cause and the consequence of the dilatation of the follicle, the case falling under the category of those circles of cause and effect with which we are familiar in the pathology of physiological cysts, *e.g.* the urinary and gall-bladders. The contents of the cyst are now friable and greasy, now more honey-like, now a stiffly gelatinous, transparent and concentrically laminated mass. On one occasion I came across a cyst which admirably illustrated the popular German name of *Grützbeutelgeschwulst.* In a thin fluid like the yolk of a raw egg, a number of grey, translucent granules, not unlike boiled groats, were suspended. All atheromatous cysts of any size usually contain cholesterin in large quantities, which gives the gruelly matter a spangled lustre. The microscope shows us that all matters resembling boiled groats or jelly, all the white, friable contents of the cyst, are made up of epidermic cells in a partial state of fatty degeneration. The yellow constituents are granule-cells and oily *débris*; the glittering scales, as has been already stated, are cholesterin-plates. We sometimes find a certain number of fine lanugo-hairs; these have obviously grown either from pre-existing or from newly-formed hair-roots. Upon the whole, the hair is strikingly passive in all disorders due to retention. At first it acts merely as a plug to complete the closure of the follicular orifice. The greater the subsequent accumulation of epidermic masses, the more does the middle part of the hair waste; its growth is either wholly arrested, or continues for a while in a meagre sort of way.

§ 334. Before leaving the present subject, some allusion ought to be made to a phenomenon, which is peculiarly frequent in association with atheromatous cysts, but which also possesses a certain degree of general interest in reference to the pathology of the hair-sac: I refer to its DISPLACEMENT.

The normal hair-sac—so at least we are taught by normal histology—is embedded in the substance of the true skin; it is only the longest and most vigorous hairs which push their roots into the subcutaneous adipose tissue. This statement needs qualification. It is true that in a cross-section through the healthy skin, the great majority of the hair-sacs really do not extend beyond the limit of the cutis. No sooner however is the hair-sac enlarged to any considerable extent, than it forces its way out of the cutis and becomes subcutaneous. Accordingly even the smaller atheromatous cysts are all situated, not in the substance of the cutis, but underneath it. We observe a precisely analogous displacement of the follicle in lupus, in hypertrophy of the sebaceous glands, &c., so that its cause is really worth inquiring into. And here an old observation of my own, which I made during the investigation of a colossal myxoma (twelve pounds in weight) from the skin of the back, comes in very appropriately.

This tumour had originated in the subcutaneous areolar tissue; the skin over it was very tightly stretched. On removing any part of this cutaneous investment and examining its under surface with a powerful lens, it became at once apparent that the hair-sacs with their appended sebaceous glands were projecting from it. Some were quite free; others lay in shallow, funnel-shaped depressions, formed by the dissociation of the fasciculi of the dermal connective tissue. The general impression conveyed was, that pre-existing recesses had been opened up from below by the stretching to which the skin was exposed, just as the mouths of the uterine glands become funnel-shaped when the mucous lining of the organ is distended from within during pregnancy. This led me to subject bits of healthy skin to a renewed examination; and I then found that wherever a hair-sac of medium or large size (I except only the smallest lanugo-hairs) was implanted in the cutis, it lay, not so much in its substance, as in a sort of prolongation of the subcutaneous connective tissue. Now should a follicle of this kind increase in size from any cause, it must separate the fibrous bundles of the corium from one another quite as effectually as dilating pressure from below; the recess is opened up; and the above-mentioned prolongation of lax connective tissue acts as a gubernaculum to guide the hair-sac in its descent into the subcutaneous tissue.*

β. *Inflammation.*

§ 335. The state of things in the interior of the hair-follicle, and especially the retention of its secretion, cannot continue without reacting on surrounding parts. We have seen that in molluscum contagiosum, as well as in atheromatous cysts, hyperplastic changes in the surrounding connective tissue were excited by the retained secretions, changes which ultimately resulted in swelling and thickening. Inflammation of the hair-sacs—or rather inflammatory processes starting from the hair-sacs—proves however, that this reaction of the environment against the morbid state of the follicle, may also assume an acute and heteroplastic character.

§ 336. What is known as ACNE, presents us with a series of anatomical phenomena, consisting essentially of retention of secreted matters on the one hand, and of a perifollicular inflammation on the other. This eruption is very common as an accidental complication of comedones and milia. It may be that the products resulting from decomposition of the stagnant contents of the follicle act as irritants upon the cutis. A more unlikely supposition is that the perifollicular inflammation is primary; that it causes swelling of the subepithelial connective tissue about the neck of the hair-sac; and so, by stopping up its mouth, brings about an accumulation of secreted matters as a secondary phenomenon. In every pustule of acne, we must distinguish anatomically between the alterations in the central hair-sac, and those in the surrounding connective tissue. The root and root-sheath of the hair remain passive throughout, save that a large number of epidermic cells in a state of fatty degeneration collect between them. All the more striking is the active part taken by the sac of connective tissue in the inflammatory process. It appears to be completely converted into pus; for in the matter squeezed from a ripe acne-pustule, I have never found any trace of it; nothing but the hair, together with the pus-corpuscles and epidermic cells; and this although the residual loss of substance is twice or three times as large as the original hair-sac. The vessels of the follicle, owing to the liquefaction of the connective tissue in which they lie, undergo maceration; the cells which line the sac appear to share in the inflammatory proliferation, and the walls of the sac to lose their cohesion in consequence; for when the escape of the pus relieves them from compression, they nearly always give way.

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* *Wertheim* had already pointed out (in 1864) the mode of implantation of the hair-sac, and shown that it passed directly into a fasciculus of connective tissue coming from the deeper layers. (On the Structure of the Hair-Sac in Man, &c. Sitzber. der Kais. Akad. Bd. L. April.)

The true seat of inflammation is the surrounding connective tissue of the cutis; hyperæmia, plastic infiltration, and suppuration, following one another in an area extending from half a line to two lines from the follicle. The pus collects round the latter, and long before we can detect it shining through the cuticle, a drop of it exists in the depths of the corium, which may be evacuated by a puncture (*G. Simon*). It is not till a later period, that the little abscess begins to point. The mouth of the follicle opens very gradually, the bundles of connective tissue which surround it yield very unwillingly. The pus-cells burrow between them and the epidermic portion of the hair-sac, and accumulate round the shaft of the hair, pushing the epidermis before them. Finally, the process culminates in the speedy rise of a somewhat abrupt, straw-yellow pustule. If the pustule be punctured and kept from drying up, it gradually empties itself of its own accord. As a rule, a firm pinch expels both the pus and the follicle which contains it. The proliferative activity in the skin rapidly subsides thereupon; the bundles of connective tissue come together again, and the little hollow which was formerly occupied by the follicle is filled up with a small quantity of cicatricial tissue.

Sycosis is merely a variety of acne. While the latter is chiefly confined to those regions of the skin which are coated with down only, the former attacks the hairy scalp, the beard, the eyebrows, &c. No previous retention of secreted matter in the affected follicles can be shown to occur. *Köbner* finds the source of irritation in a vegetable parasite which invades the hair-follicle; I agree with *Hebra* in believing that this parasite is very seldom to be found.

§ 337. The assumption that FURUNCULAR INFLAMMATION invariably starts from a hair-follicle, is certainly not universally received; every one must admit the occasional possibility of such an origin; and if it be an accident, it is undoubtedly a very singular one, that I myself should never have been fortunate enough to meet with any other mode of origin. Considering how common furunculi are, it is clearly easy to get any quantity of the so-called "cores" for examination. These, however, do not suffice to decide the vexed question as to the origin of the inflammatory process. For this purpose it is necessary to have recent specimens with the whole of the neighbouring skin for examination; and these are not readily to be had. Whenever I had an opportunity of examining such materials, I invariably found, in the focus of inflammation, one of those funnel-shaped protrusions of the subcutaneous connective tissue into the cutis, which serve, as has already been shown, for the reception of hair-sacs (§ 334). *Bardeleben's* account is very similar (*Bardeleben*, Lehrbuch der Chirurgie, vol. ii. p. 17).

Furunculi differ from acne and sycosis in the extent of the inflammation; this is not confined to the substance of the cutis, but, though reaching its maximum intensity in that structure, spreads at the same time into the subcutaneous connective tissue. Once upon this very irritable soil, the inflammation rapidly extends over disproportionately large areas. The hyperæmia, together with a vigorous lymphatic saturation, suffice of themselves to cause the nodular swelling (perhaps as large as a pigeon's egg), which can be felt through the tense and diffusely reddened skin.

In marked contrast to the wide extent of these preliminary stages, the inflammatory proliferation is really confined within narrow limits. It extends but a little way from the circumference of the above-mentioned protrusion of subcutaneous connective tissue into the substance of the cutis. Within this area, however, the plastic infiltration assumes such proportions, the accumulation of pus-cells is so dense, that the blood-vessels undergo compression. In one variety of the furunculus, the ANTHRAX, this goes so far as actually to cause the death of the infiltrated part, which grows as black and dry as boot-leather; in ordinary furunculi the process does not go beyond simple necrobiosis; many of the cells show signs of fatty degeneration. In either case, however, the infiltrated part is gradually cut off from the surrounding connective tissue by a process of suppurative demarcation, and expelled from the skin—a termination usually hastened by operative interference. It constitutes the familiar "core" which, when teazed out under the microscope, exhibits nothing beyond disintegrating cells and a few fibres of connective tissue amid a mass of *débris.* After the expulsion of the core the sinuous ulcer which remains, heals by the second intention, leaving a stellate scar.

γ. *Hypertrophy.*

§ 338. Active enlargements of the hair-follicles, due to morbid growth, must be distinguished from their passive enlargement, due to retained secretions. Next, they must themselves be divided into true and false hypertrophies; the former retaining the original anatomical and physiological character of the parts; while in the latter, the increase in size is associated with some specific modification of structure which arrests their normal functional activity. The hair-sacs and their appended glands thus become foreign to the organism; they pass into the category of heteroplastic tumours. The consideration of these "false" hypertrophies will therefore be deferred for the present.

§ 339. A true "OVERGROWTH OF HAIR" can only be said to exist in hairy moles, the so-called "mice" (*nævus spilus*). These brown, hemispherical or flattened elevations of the skin, sometimes of considerable size, would seem to offer peculiar facilities for the most luxuriant growth of hair. Not only are the individual hairs very stout, but, if we happen to possess a mole of our own, we notice that its hairs are shed and renewed much oftener than those of the head and beard. If we make a vertical section through one of these nævi, we find at least one-fourth of the hair-follicles, which are very thickly set, furnished with a little accessory sac occupied by a new hair in a more or less advanced stage of development; we find the appearances which *Kölliker* has figured in his Handbook (figs. 79 and 80). I cannot but seek the essential feature of the *nævus spilus* in this overgrowth of hair. The sebaceous glands are in nowise implicated.

§ 340. Once, and once only have I met with a true OVERGROWTH OF THE SEBACEOUS GLANDS, and I question whether the growth described by *Förster* under the name of "glandular tumour" of the sebaceous follicles is a true hypertrophy at all, since it exhibits a certain rodent tendency which is only associated with the false hypertrophies, with lupus and cancroid. The tumour which I examined was sent me by Professor *Wernher* of Giessen; it was as big as a pigeon's egg, and attached by a broad base to the hairy scalp; it was freely moveable. The skin over it was pitted; the holes could be seen with the naked eye; they were the mouths of hypertrophied sebaceous follicles; no hairs were present.

Sections of the tumour forcibly reminded me of similar sections from a normal mammary gland. Amid the thick trabeculæ of a very tough stroma, there lay acini consisting of from three to five terminal follicles with a common efferent duct; among these were scattered wider ducts, cut across transversely and obliquely. Each acinus contained very small, round, epithelial cells; the ducts were filled with solid and liquid fatty matter. The growth as a whole was of a homologous character; it was nothing more than an overgrowth of the normal type of a sebaceous gland, similar to that which is normally carried out in the mammary gland.

§ 341. This is the place to say a few words about a true HYPERTROPHY OF THE SUDORIPAROUS GLANDS, by way of appendix to the present section; for I do not intend to devote a separate chapter to these structures. The false hypertrophies of the sweat-glands, like those of the sebaceous follicles, fall under the head either of epithelioma or of lupus. True hypertrophy of the sudoriparous glands gives rise to a flat, fungoid elevation of the skin, which, smooth and hairless, is not unlike a soft wart. On cutting into it however, we see at once that neither the papillary body, nor any other part of the cutis, is involved. The sweat-glands, as everybody knows, lie at the junction of the skin with the subcutaneous connective tissue; it is here therefore that the main body of the tumour is really situated; it consists of a pad of sweat-glands, from three to four lines in thickness, and of corresponding width. Each single gland may attain to the diameter of one line; the adipose tissue seems to be partly pushed aside, while the bands of connective tissue between the individual glands are thickened.

The occurrence of small cysts, full of clear mucus, must be regarded as a sign of retrograde metamorphosis. They originate in the total liquefaction of single glands, and occupy exactly the same space.

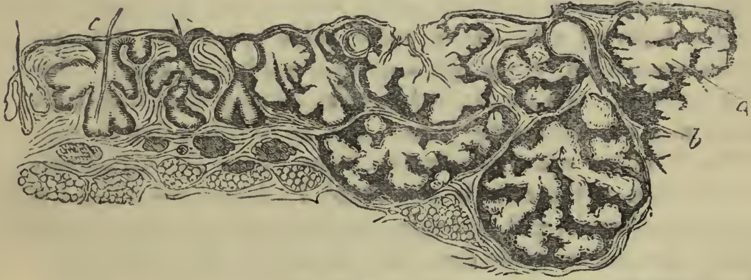
δ. *Heteroplastic Tumours.—Lupus.*

§ 342. The undoubted participation of the hair-sacs and sebaceous glands in the genesis of epithelial cancer was satisfactorily proved in § 166. The hair-sacs and sebaceous glands were shown to behave just like all other protrusions of the epidermis into the cutis; like the sudoriparous glands, and the downward processes of the rete Malpighii which occupy the interpapillary furrows. There exists, however, a true adenoma of the sebaceous and sudoriparous glands, a tumour which, in common with all adenomata, is closely related to epithelial cancer, but which differs from it, like all other adenomata, partly in its structure, partly by its more local and ametastatic character: I refer to LUPUS.

§ 343. If my views of lupoid growth should seem to be more in accordance with the older than with the more recent observations on the subject, this is probably due to the great reluctance of recent authors to see anything peculiar in lupus, any departure from the common type of inflammatory growth. In reality the lupoid tubercles are so characteristic, not only in their mode of origin, but in their structure also, that I readily pledge myself to recognise lupus, quite as certainly as cancer, by microscopic analysis alone. It is true that the cells of the lupoid tubercle are, on the whole, of small size and round, that they are closely packed, and held together by a mucoid cement; so that if it were desired to find a name for the tissue of which they consist, that of embryonic tissue might well be chosen as the fittest. But ought we on that account to neglect the manifold variety of internal structure, and the very singular mode of origin, of this embryonic tissue?

First, as to structure. Every lupoid tubercle, whether it be situated in the cutis or in the subcutaneous connective tissue, presents a well-marked acinous composition. This is easily proved by examining sections of a piece of skin infiltrated with lupus, after it has been hardened in alcohol, steeped for eighteen hours in a strong solution of carmine, and finally cleared up with appropriate agents, among which Canada balsam is the best. In the smaller tubercles we distinguish from two to three, in the larger ones—those about the size of a hemp-seed—from seven to ten roundly-oval, tortuous bodies, everywhere studded with roundish projections; these bodies are bulbous at one end, tapering off at the other to converge towards a common centre (fig. 120, *a*). These bodies are made up of cells of considerable size, whose protoplasm has resisted the carmine, and which accordingly appear white, in marked contrast to the remaining parenchyma of the nodule in which they are embedded. This residual parenchyma (fig. 120, *b*) consists entirely of true embryonic tissue; the cells are small, perfectly round, lustrous and readily tinted by carmine. Here too the vessels of the lupoid nodule, as described by some authors, ramify: they form a network round the bulbous ends referred to above, towards which they stand in the same relation as that taken up by the vessels towards the terminal follicles of an acinous gland, thus confirming my view of the acinous structure of the lupoid nodule.

FIG. 120.



Lupus. Vertical section, showing the passage of the healthy skin into that which is most infiltrated. *a*. Acinous nodules; *b*. Embryonic tissue of the lupus-nodule; *c*. Altered hair-sacs and sebaceous glands. $\frac{1}{10}$.

§ 344. We have next to ascertain the cause of these highly characteristic appearances; the notion that the acinous composition of the nodule may be due to the degeneration of some pre-existing structure of the same sort—such as that of the sebaceous glands—suggests itself spontaneously. Now if we make vertical sections through the advancing border of the lupus, sections which include both healthy skin and that which is completely diseased, we see at a glance, that the sebaceous glands do really take a very important part in the disease. It has long been known that at the extreme periphery of the affected region they swell up and shine through the cuticle as white nodules. This swelling is due, partly to a proliferation of the glandular elements, partly to the fact, that instead of undergoing fatty degeneration, the cells grow large and vesicular, distending the body of the gland even to five times its normal bulk. The root-sheath of the hair also takes part in this degenerative change by producing, instead of the usual flattened epidermic cells, large vesicular corpuscles like those produced by the sebaceous gland. This productive activity, however, is not as a rule exhibited by the entire root-sheath in the same degree; it is now confined to the fundus, now it involves the fundus together with one or more points above it; this very soon gives the hair-sac proper a varicose and knotty aspect. The hair perishes. Glands can no longer be distinguished from hair-sacs; they are all exactly alike. Yet up to this point the condition is in no sense peculiar to lupus; since the metaplastic enlargement of the cells is also found in the neighbourhood of leprous, syphilitic, and especially epitheliomatous diseases of the skin. The characteristic part of the disorder is that which immediately ensues.

§ 345. Lupus has been held on various grounds to be a proliferation of the corpuscular elements of the rete Malpighii (*Berger*, Dissertatio inaugur. Greifswald; and *Pohl*, *Virchow's* Archiv, Bd. vi.). I may be said to agree with this view in one sense, inasmuch as I too seek to localise the proliferation at the junction of the epithelial and connective-tissue layers; but I do not limit it to the rete Malpighii, *i.e.* to the boundary-line between connective tissue and epidermis in its stricter sense; on the contrary, I regard it as concentrated in the glandular inflexions of the epidermis. The process begins as a luxuriant corpuscular proliferation in the interstitial and capsular connective tissue of the sebaceous and sudoriparous glands. This proliferation extends to a variable distance into the surrounding parts; its progress may be admirably watched in the adipose tissue which invests the deeper sweat-glands; little round corpuscles make their appearance between adjacent fat-cells, which they engirdle, before entirely covering and masking them from view. On the other hand, the cell-growth often extends deep into the subcutaneous connective tissue along the afferent vessels; in the interior of the gland itself, the mass of newly-developed embryonic tissue also exhibits a dendritic arrangement, the parent-trunk coinciding with the point of entrance of the afferent vessel.

In proportion to this exuberant cell-growth at the periphery of the glandular tubes and acini, the latter themselves increase in bulk; their shape is altered, they become knotty and bulbous, as described above; their cavities are obliterated, and only their general arrangement can be traced; the parenchyma being grouped round a central point which corresponds to the efferent duct. The cells of which the degenerated acini consist, are not the same large, vesicular elements, which took up so much space during the stage of primary enlargement. Their size is only about double that of the embryonic cells; they are concentrically aggregated into little groups; we notice indications, as it were, of a tendency towards a higher degree of epithelial development; but the cells never get beyond the stage of those which make up the rete Malpighii.

§ 346. It may be objected that lupoid nodules are not always superficial, that they are often met with deep in the subcutaneous connective tissue. To this objection I rejoin, that the sweat-glands, in particular, may even normally lie very deep, and that as they increase in size, they are necessarily dislocated in a downward direction, just as happens in the case of atheromatous cysts. Finally, I must not omit to state that the development of granulation-tissue, in what is known as the hypertrophic variety of lupus, extends far beyond the limits of the glands, and that this granulation-tissue is capable of being converted into mature connective tissue, forming indurations like those in elephantiasis. But the lupoid nodule proper is always an adenoma of a sebaceous or sudoriparous gland.

The further destiny of the lupoid products is usually this: the parenchyma proper undergoes fatty degeneration while the intermediate granulation-tissue is converted into pus. The little abscesses thus formed, burst, and discharge their contents. Tumours and cicatrices follow the same law as in leprosy and syphilis.

ε. *Atrophy.*

§ 347. The falling-off of the hair of the head in OLD AGE is due to a total involution of its place of origin, *i.e.* of the hair-sacs and the roots of the hair. The former are dilated and shortened, the latter grow smaller, and either disappear or are only capable of producing and nourishing a lanugo.

PREMATURE BALDNESS is invariably connected with a disordered relation between the production of epidermic cells from the hair-sac on the one hand, and from the hair-root on the other. If cells are formed in excessive numbers by the lining of the sac, the lateral pressure to which the hair is exposed in the interior of the follicle, interferes with the nutrition of the shaft, and causes it to wither and become spontaneously detached from its root. This occurs in the "defluvium capillorum" which is met with in the course of constitutional syphilis, or after acute diseases, such as typhus abdominalis.

The second and far rarer case is when the productive activity of the root sinks below its normal standard. The hair-follicle is in nowise altered, but the normal degree of lateral pressure exerted upon the shaft by the narrowest part of the follicle (just below the point at which the sebaceous glands open into it) is too great to be overcome by the diminished upward strain of the growing hair. The latter is accordingly arrested at this point; its cells undergo a finely-granular metamorphosis, preliminary to a solution of continuity which is effected by the least traction upon the shaft from without (as in combing the hair). The remaining stump is very soft; it becomes swollen and knotty, owing to the fact that the materials furnished by the root, though inadequate for the construction of a normal hair, yet form, in course of time, a shapeless corpuscular aggregate of considerable size. (*Alopecia areata. Area Celsi.*)

V.—MORBID ANATOMY OF MUCOUS MEMBRANES.

§ 348. From the mouth to the anus, there extends a system of membranous canals, which, owing to their free surface being always moist, and coated with a thin layer of mucus, have received the name of the MUCOUS SYSTEM. The membranous walls of these canals are in direct continuity with the skin; like the skin, they serve to shut off the organism from its environment—the I from the not-I; this must always be kept in view; we must bear in mind, for instance, that whatever a man may have taken into his stomach, is still only at the gates of the organism, not in its interior. Not only is the skin continuous in a general way with the mucous tract at the oral, nasal, ocular and aural apertures, at the anal, urethral and vaginal orifices, but each individual layer of the skin may be traced into a corresponding layer of the mucous membrane; the epidermis into the epithelium, the cutis into the mucosa proper, the subcutaneous into the sub-mucous tissue.* Moreover each layer retains its general character; the epithelium continues to serve as a protective covering which shuts off the organism against the world without, the mucosa represents the proper connective tissue of the mucous membrane, the submucous is a lax areolar tissue which facilitates the movements of the mucosa upon the muscular coat. But within these limits of homology, both the structure and the functions of each layer are modified in accordance with the physiological duties of the various divisions of the mucous tract.

First, as regards the epithelium. At all the mucous orifices the horny lamina of the epidermis disappears, so that the atrial chambers of the mucous tract (the buccal cavity, pharynx and œsophagus, conjunctiva, vulva, preputial sac, bladder and ureters) are lined only by the mucous layer of the cuticle, the so-called laminated pavement-epithelium. This laminated pavement-epithelium consists, like the rete Malpighii, of a single layer of small, columnar cells, and a stratum of variable depth of larger pavement cells, which grow flatter as they approach the free surface, where they are finally shed.

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* The fourth layer of the mucous tract—the muscular coat—does not form any part of the mucous membrane proper; it corresponds to the locomotive apparatus of the body in its entirety, to the osseous and muscular systems; the fifth layer consists in either case of serous membrane, forming on the one hand the visceral, on the other, the parietal lamina of the same serous sac.

As regards the meaning of this diminution in thickness of the epithelial layer in the vestibular portions of the vegetative tract, there cannot be two opinions. It is the first step towards an increased facility of osmotic interchange between the fluids and gases contained in the cavity, and those contained in the blood. Wherever such interchange is more active, wherever absorption or secretion are going on, wherever it lies at the root of the general nutrition of the organism, the pavement cells disappear entirely, and the columnar cells alone remain. Thus the alimentary canal from the cardia to the anus, the respiratory passages, the female generative organs from the external os inwards, are lined with columnar epithelium. Its cells are larger than the columnar elements of the rete; they exhibit manifold varieties of external form, in accordance with the functional necessities of particular regions; inasmuch, however, as they are planted immediately upon the connective tissue, and as between their bases only a few reserve cells, to replace those which are shed, are here and there apparent—cells which might certainly be demonstrated in the rete Malpighii also—I cannot see any objection to their being viewed as the anatomical equivalent of the columnar cells of the rete, notwithstanding any modifications of size and form which they may present.

Like the epithelium, the proper substance of the mucous membrane undergoes adaptation to the special functions of the individual portions of the tract. In parts devoted merely to the transmission and storage of their contents—in the œsophagus, biliary and urinary passages, vagina, &c., we find an equable layer of tough fibrillæ of connective tissue, terminating in a smooth and even surface underneath the epithelium, while on the other side it is uninterruptedly continuous with the bundles of the lax submucous connective tissue. Its texture is very different where the tract is devoted to absorption or secretion.

Here the mucosa lodges the most important glandular organs, while its surface and its component tissues are modified in accordance with the functions which it has to perform: *e.g.* for purposes of absorption it is important that as wide an area as possible should be brought in contact with the chyme; we find this requirement met by the villi with which the alimentary mucous membrane is beset from the duodenum downwards, each villus containing a lymphatic radicle in its axis; and in order still more to facilitate absorption, we find the layer of connective tissue which intervenes between the vessels and the epithelium, presenting in a very high degree the properties of lymphadenoid tissue, with whose structure we first became acquainted in the lymphatic glands. The absorbent apparatus includes moreover the numerous follicular (conglobate, *Henle*) glands; the solitary glands, the patches of *Peyer*, the tonsils, and the saccular glands at the root of the tongue. These may be said to form the first stage on the road, which the matters to be absorbed by the lymphatic system have to traverse. Should these matters happen to be pathological irritants, their path is marked by hyperæmia, inflammation and morbid growth; hence it is, that in so many of the general disorders of the entire alimentary tract, we find these follicular structures peculiarly involved.

Of the secreting glands, it is only the smaller ones, the simple tubular glands, which are situated in the thickness of the mucous membrane, while those of larger size, the follicular mucous glands, are mainly embedded in the submucous tissue. Nevertheless, some mucous membranes are inordinately rich in glandular structures; *e.g.* the gastric mucous membrane has five-sixths of its bulk made up of gland-substance.

About the submucous tissue there is not much to be said; we shall find it a peculiarly favourable locality for the development and spread of morbid growths, when these come to be discussed.

a. INFLAMMATION.

1. *Catarrhal Inflammation.—Catarrh.*

§ 349. The larger half of all the diseases to which humanity is liable, consists of catarrhal affections of mucous membranes, or of disorders complicated by them. The term "catarrh" lays stress on only one, though certainly the most prominent phenomenon of the disease, *sc.* the increased secretion from the mucous surface. We must bear in mind, however, that the increased secretion can never occur without a simultaneous hyperæmia of the mucous membrane, and that this hyperæmia is the proximate cause of the increased secretion, and the more or less remote cause of farther troubles, of swelling, hæmorrhage, pigmentation, hypertrophy, &c., all of which must be included in any complete view of the morbid anatomy of mucous catarrh.

Hyperæmia must accordingly be regarded as the anatomical basis of catarrh. It may either be active or passive. In the former event, it is the primary result of some antecedent irritation; in the latter, it lasts for a long time before catarrhal inflammation is set up—it acts as a predisposing cause; (I am thinking of the bronchial catarrh of heart disease, of the gastro-intestinal catarrh associated with portal obstruction, of the catarrhal affections of the rectum and bladder due to piles). Whether we are justified in assuming that the catarrh is actually excited in these cases by some special exacerbation of the existing hyperæmia, or even by some modification in its passive character, I cannot take it upon me to decide. To my mind, it appears more profitable to inquire how far, and in what localities, the normal structure of the mucous tract favours the origin or the continuance of hyperæmia. And first, we must recollect that owing to the tenuity and permeability of the epithelial stratum, the access of external irritants to the irritable elements of the mucous membrane is far easier than in the skin; moreover, that there is no elastic covering, like the horny lamina of the cuticle, to check the turgescence of the capillaries; nay, the softness of the parenchyma sets no limit to their distension. The relations in which the contractions of the muscular coat of the bowel stand towards the distribution of blood in the mucous coat, are of peculiar interest. The small arteries and veins, which carry the blood to and from the capillary networks of the gastro-intestinal mucous membrane, penetrate, as is well known, obliquely through the muscular coat. Here they receive a sheath of loose connective tissue, which, in the case of the arteries, is tolerably wide, so that a considerable space is left between the vessel and the muscular fasciculi; in the case of the veins, on the other hand, it is exceedingly slight; these are accordingly liable to be compressed, whenever the muscular coat contracts. Hence every such contraction must hinder the efflux of blood from the alimentary mucous membrane; its vessels are congested, the congestion lasting as long as the contraction, and being liable to assume a more chronic character if the contractions are often repeated. The bearings of this arrangement upon the digestive process are very obvious. The peristaltic contractions, besides pushing on the contents of the bowel, help both secretion and absorption by exciting and keeping up a hyperæmic state of the mucous membrane; they aid secretion, by supplying the open glands with raw material in greater abundance; they help absorption, by causing that injection of the capillaries of the villi, which, according to *Kölliker*, co-operates so weightily towards the filling of the axial lymphatic space. Meanwhile, we must remember that every physiological hyperæmia is a gift of the Danai to the organ which is liable to it; since the least derangement of the machinery converts its benefits into curses. So in the present case. No mucous membrane exhibits catarrhal disturbances of circulation in so intense a degree as that of the stomach and intestines; for the irritant which affects the mucous membrane excites peristaltic contraction quite as promptly, and far more powerfully, than the food. Dysentery and cholera afford colossal examples of the harm which may accrue in this way; the intense œdema of the mucous membrane of the large intestine in the former disease, the hæmorrhages, even the diphtheritic lesions, are partly due to the violent tonic spasm of the muscular coat; and if we go on to assume that in cholera, an excess of peristaltic activity contributes in some measure towards the copious flux from the gastro-intestinal surface, we shall have got at a causal nexus between two of its most familiar symptoms. But we need not go so far afield in search of illustrations; the phenomenon exhibited on so great a scale by cholera and dysentery, is repeated on a small one in every catarrh, however trifling. We shall come across it again when we discuss the pathology of hæmorrhage from mucous surfaces, and that of gastric ulcer (perforating ulcer of the stomach).

It is only the vesical and uterine mucous membranes which are subject to similar conditions. Menstruation is associated with clonic contractions of the muscular coat of the uterus.

Some mucous membranes, however, are not well adapted for the occurrence of hyperæmia. The more abundantly a mucous membrane is provided with elastic fibres, the more does it resist distension by congestion and œdema; indeed the tendency of the membrane to return to its normal volume, increases in proportion to the stretching which it undergoes; this is a necessary result of its elasticity. Many of the phenomena exhibited by the respiratory mucous membrane, which is peculiarly rich in elastic fibres, must be ascribed to this cause. Sudden and great swelling only occurs in parts furnished with a very lax submucous areolar tissue, in the folds about the laryngeal orifice, particularly the ary-epiglottidean ligaments, and certain portions of the mucous lining of the nasal cavities. The swelling in such cases however, is not situated in the mucosa; it is due to œdema of the submucous connective tissue. It disappears very rapidly as soon as the elastic reaction of the stretched membrane prevails over the tension of the dropsical effusion kept up by the blood-pressure; especially after death, when it is often quite impossible to demonstrate the existence of an œdema, which manifested itself most unequivocally during life, and which may even have been the cause of death (œdema glottidis).

§ 350. It is obvious that the SWELLING of the catarrhal mucous membrane, the second anatomical element in this variety of inflammation, depends, at least in some degree, upon the hyperæmia; *i.e.* so far as it is due to over-distension of the vessels, and the abundant saturation of the mucous membrane with serum. The latter element is very prominent in all forms of catarrh due to passive congestion; it is recognised by the bacony lustre of the swollen membrane, and by the flow of clear serum from its cut surface. The swelling is much greater when the submucous tissue also is involved; this is most common in the cæcum.

For the pathological histologist, these passive forms of swelling are less interesting than the active varieties; *i.e.* the enlargements of the LYMPHATIC FOLLICLES due to corpuscular proliferation in their interior. Owing doubtless to the intimate connexion of these glands with the process of absorption, we find catarrh of a mucous surface almost always associated with a more or less extensive implication of those lymphatic structures which are traversed by the lymph returning from the affected membrane. The first to become involved are the follicles embedded in the substance of the mucous membrane; the lymphatic glands proper, which lie outside the mucous tract, come next, and that in the following order: in catarrh of the nasal, pharyngeal and buccal cavities, the glands of the neck; in catarrh of the respiratory tract, the glands about the root of the lungs and the bifurcation of the trachea; in catarrh of the digestive tract, the mesenteric glands; in catarrh of the genito-urinary apparatus, the retroperitoneal and inguinal groups of glands.

As regards the process itself, it is essentially a form of acute suppurative lymphadenitis, described at length in § 200 *et seqq.* Its simplest and least complicated manifestation is the *follicular suppuration of the gastro-intestinal mucous membrane.* The violent catarrhal disorders of the intestine, which occur during the height of summer, occasionally exhibit all stages of the process at once; its beginnings may also be studied as intercurrent or prodromal phenomena in tuberculosis, enteric fever, Asiatic cholera, and dysentery. The swelling usually begins with a marked congestion of the perifollicular blood-vessels; the general hyperæmia seems to concentrate itself round the follicles; this hyperæmia may be partly collateral, due to the impeded access of blood to the follicle itself. The solitary gland presents itself as a dull-grey, pearly nodule, as large as a pin's head, surrounded by a vascular ring. A Peyer's patch in this condition is a most beautiful object; the hyperæmic areolæ of its constituent follicles being in contact with one another. When suppuration occurs, the follicle swells to the size of a small pea; its site is indicated by a yellowish, fluctuating point, over which the outer layer of the mucosa is moderately stretched. If the pus is let out, the roof of the cavity falls in, and a slight hollow is left. A stream of water distends the cavity once more, and enables us to appreciate its striking dimensions. These can only be accounted for by assuming that the perifollicular connective tissue has become involved in the suppurative process. For, so long as the pus remains enclosed in the parenchyma of the mucous membrane, it exerts—if I may be allowed the comparison—a catalytic action upon the connective tissue which immediately surrounds it. Hence we not unfrequently find the contiguous follicular abscesses of a Peyer's patch communicating with each other by fistulous passages under the mucous membrane; the latter may be undermined in this way to a considerable distance. The roof ultimately dies; it becomes detached at its edges, and the loss of substance resulting from the ulceration, manifests itself as a sharply circumscribed, round or roundish ulcer. Cicatrisation usually follows without any difficulty; yet I myself have seen a perforation of the bowel just above the ileocæcal valve.

Follicular swelling and ulceration of the stomach, necessarily presuppose the existence of follicles in the gastric mucous membrane. Now it is well known that in some stomachs not a single follicle can be discovered. As regards the stomach, we might perhaps be justified in speculating whether a special development of follicles *ad hoc* might not occur, somewhat after the fashion in which *Henle* assumes the "conglobate" glands to originate. The formative irritation to which the connective tissue of the entire mucous membrane is subjected, becomes as it were concentrated in a series of foci, just as a cutaneous exanthem is limited to a certain, though often very large, number of definite centres. About the law which regulates this distribution we know nothing. Characteristic of this affection, when it occurs in the stomach, is the circumstance that all the follicles are invariably found in the same stage of transformation, whether as grey pearly nodules, as abscesses, or as ulcers.

§ 351. The analogous conditions of the TONSILS are somewhat more complex. The hemispherical surface of these organs presents, as we know, a certain number of pouch-like depressions. These depressions are lined by the pavement-epithelium of the oral cavity; little papillæ, like the lingual papillæ in miniature, are often found growing in the neck of the pouches. Around them, embedded in the mucous parenchyma, lie the lymphatic follicles. They are separated from the surface by a thin layer of connective tissue, and are not therefore in contact with it (as in the sheep, *Frey*). Now in catarrh of the pharynx with angina tonsillaris, an increased production of epithelium takes place not only on the tongue (furred tongue), but on the inner surface of these depressions also. A quantity of pavement-epithelium consequently accumulates in their interior; a white, greasy mass, not unlike the *vernix caseosa* of the fœtus, forms a largish plug, which projects from the mouth of the pouch, but does not, however, escape from it; this alone contributes in no small degree to the enlargement of the entire tonsil. Add to this the inflammation and suppuration in the follicles. One after another (for they do not all appear to be affected at once) they swell and soften. The contiguous abscesses run together here and there, until at last (supposing the natural order of events not to be forestalled by interference with the knife or caustics), the entire tonsil is excavated by a sinuous abscess, which is converted, when the pus escapes, into a sinuous fistula. This usually occurs at several points at once. Thereupon the gland suddenly collapses; always supposing that the follicular abscesses have previously become confluent. In the contrary event, those follicles which have not yet burst, together with those which have entirely escaped the disease, undergo no further change, and represent what is left of a tonsil. The fistulous sinus, as a rule, is speedily filled up by cicatricial tissue, without the occurrence of any dangerous complication. Should the healing process be delayed, should the base of the ulcer assume a gangrenous and putrid character, the proximity of the internal carotid becomes a source of danger; intractable hæmorrhage may result, when the vessel is laid bare by suppuration and then perforated. (*Hæmorrhagia per diabrosin.*)

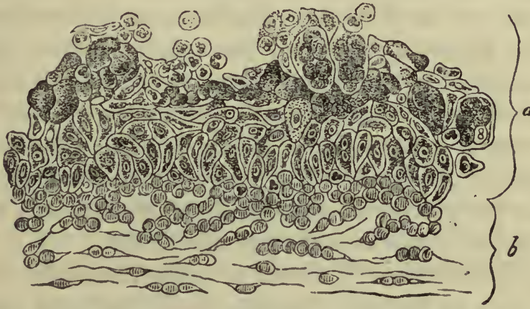
§ 352. The changes which the SECRETIONS of the mucous membrane undergo, under the influence of catarrhal inflammation, are so striking, and afford such weighty indications for clinical diagnosis, that catarrhal disorders have been summarily defined by more than one author, as anomalies of secretion. This is an error, inasmuch as the morbid state of the secretions is not the cause, but the consequence of the catarrh. It would be quite as incorrect to see nothing in a catarrh beyond a quantitative increase of the normal secretion. One secretion may differ from another, and this difference is very manifest in the present case. Those secretions of the mucous tract which are most important physiologically, the gastric and intestinal juices, are not by any means more abundantly secreted by the catarrhal than by the healthy mucous membrane; on the contrary, a diminution in the amount of these secretions may be expected as an invariable functional concomitant of catarrhal inflammation. This statement does not apply in the same degree to the ordinary mucus, of minor physiological importance, with which the mucous membrane, even in its normal state, is coated. We are familiar with "mucous catarrhs" in which mucus is secreted in excessive quantity. They chiefly affect such parts of the tract as are distinguished by their wealth in muciparous glands, *e.g.* the pharynx, air-passages, stomach and large intestine. We know, however, that the faculty of producing mucous is not peculiar to the acinous glands; but that mucous metamorphosis of the protoplasm is to the epithelial cells of mucous membranes, what horny transformation is to the corpuscular elements of the epidermis (cf. § 40); hence we are not surprised to find mucous catarrh, and mucoid elements in the catarrhal secretions, of mucous membranes which, like that of the bladder, are destitute of glands.

An over-production of "corpuscular" elements upon a mucous surface, presupposes a degree of irritation more intense than that which gives rise to the simple mucous variety of catarrh. Here we must distinguish between EPITHELIAL and PURULENT catarrh, according as epithelial cells or pus-corpuscles predominate in the secretion. I say predominate; since both are usually present together. A catarrh exclusively epithelial may be seen on the mucous lining of the tongue, the "fur" being nothing more than an exuberant desquamation of pavement epithelia, such as are proper to this region of the mucous tract. With regard to the origin and secretion of these cells, I refer the reader to the details given in § 83. There is no reason to suppose that the epithelial cells which are produced in excessive amount, originate according to other than the usual laws; from this point of view therefore, epithelial catarrh may be regarded as a simply hyperplastic process.

But what are we to say when we find pus-corpuscles in the catarrhal secretion, when the catarrh is purulent? Are the pus-cells also to be regarded as products of the subepithelial connective tissue? Against this view, which was formerly generally received, it may be urged, that it is always possible, either by scraping, or in vertical sections, to demonstrate an epithelium which differs little, if at all, from the normal type, in mucous membranes which are in a state of well-marked purulent catarrh. Recent researches indeed, in which *Remak*, *Buhl*, and myself have taken part, point to the conclusion that pus *may* be produced on mucous membranes by endogenous proliferation of the surface epithelia. I have already described this mode of origin in § 68. As regards the exact point where it is produced, our only guide is the arrangement of the brood-cells, as seen in vertical sections. Fig. 121 represents very accurately the mutual relation of parts as seen in the ocular conjunctiva. The mother-cells appear *in situ*, in the outermost layer of the epithelial stratum; below and on each side of them are epithelium-cells, some normal, others which have already entered upon morbid change; towards the free surface we note the liberation of pus-corpuscles, and the catarrhal secretion.

This does not prove that *all* the pus-corpuscles contained in the catarrhal flux, or that the pus-corpuscles in *all* cases of catarrh, originate in this wise. On the contrary, if we reflect that all young cells have the power of spontaneous locomotion, and that the strong current of transuding fluid may help, but cannot hinder them in their migration, we cannot believe it otherwise than possible, nay, even highly probable, that the elements of the subepithelial embryonic tissue, to which allusion has been already made, penetrate outward between the epithelial cells, and so come to be set free.

Fig. 121.



Purulent catarrh of the conjunctiva. *a*. Epithelium. *b*. Connective-tissue stratum of the mucosa.

§ 353. Mucus and cells are products of the mucous membrane; they represent the increased amount of pabulum which has been supplied to it, after it has undergone a certain elaboration into secondary products. The case is different in many catarrhal disorders of the gastro-intestinal tract. The stools of ordinary diarrhœa are due to a "serous" transudation into the small intestine. The serum of the blood, with its albumen and salts, has passed directly from the vessels of the villi to the surface; it has been forced so rapidly down the bowel by violent peristaltic movements, that the absorption in the large intestine has not been able to keep pace with it. Choleraic catarrh differs from ordinary diarrhœa, partly by the absence of albumen from the transuded fluid (in cholera this consists entirely of water and sodium chloride, *Schmidt*); partly by the implication of the whole tract from the cardia to the anus; finally by the volume of the transuded fluid, and the rapidity with which it accumulates. This rapidity is occasionally so great, that the epithelium of the small bowel, together with the epithelial lining of the follicles of *Lieberkühn*, is stripped off and swept away in shreds of variable size (rice-water evacuations). On one surface of these shreds, we see the long epithelial casts of the villi projecting like the fingers of a glove; the opposite surface exhibits the shorter and more globular outlines of the crypts of *Lieberkühn*. The intestinal mucous membrane is left as if "flayed," and is exposed without protection to the hostile action of its contents; a circumstance which must not be forgotten in endeavouring to account for the patches of superficial gangrene, which the bowel usually exhibits in the second stage of cholera.

The "hæmorrhagic" form of catarrh differs from the "serous" flux in the fact that the blood itself, and not merely some of its constituents, appears on the surface of the mucous membrane. It is usually extravasated at the most prominent points; in the stomach, on the little bridges of connective tissue which surround the orifices of the glands; in the small intestine, at the tips of the villi, and especially of those villi which beset the borders of the folds of *Kerkring;* in the ileum and colon, the parts surrounding the follicular glands are chosen; in the colon moreover, the *plicæ sigmoideæ.* The process itself consists in what is known as "diapedesis." The blood forces its way in minute quantities through correspondingly minute rents in the flexures of the capillary loops, first into the parenchymatous connective tissue, and then on to the free surface. Should the bleeding be arrested, some of the extruded blood-corpuscles are retained in the parenchyma, where they are converted into a brown or black pigment. Accordingly the mucous membrane comes to exhibit throughout, a brown, yellow, grey, or even black hue; the distribution of the pigment following the law which has just been set forth; it is only in rare and very severe cases that it is more uniformly distributed, so that the stomach, for instance, looks as if it had been flooded with ink.

§ 354. A series of peculiar phenomena is due to the possibility of serous transudation from mucous membranes lined with laminated pavement-epithelium. The outermost, compact layer of cells, resists the passage of the serum for a time; it is stripped from its bed, and so forms vesicles or bullæ. Accordingly, in catarrhal affections of the buccal cavity, we not unfrequently see the mucous membrane of the lips, gums, tongue and cheeks studded with transparent, watery blebs, some as large as a pea, while the majority are no bigger than a millet-seed; in about twenty-four hours' time they burst and discharge their serous contents. Here the matter may end; or the raised portion of epithelium may become altogether detached, leaving a small, circular defect, an excoriation, behind. The denuded patch of mucous membrane proceeds to secrete pus; its epithelial border becomes sodden, and appears to the naked eye as a sharp, white margin; the entire patch is surrounded by a hyperæmic areola, and the circumscribed purulent catarrh lasts until the cessation of the general catarrhal state. These "ulcers" may increase considerably in size; the greater part of the buccal surface may thus come to be quite raw, while the smaller part continues normal (scurvy, putrid stomatitis).

Analogous conditions are met with in all the atrial chambers of the mucous tract (see § 348). We are most familiar with those about the os uteri externum and the glans penis.

§ 355. *Complete and incomplete degeneration, chronic catarrh, and hyperplastic conditions of the mucous membranes.* What has been said above concerning catarrhal inflammation, refers to its acute variety, which runs a definite course. After this is completed, the mucous membrane may return entirely to its normal state. In this connexion, the behaviour of the parenchymatous connective tissue of the mucous membrane is most important. We have already seen (§ 352) how actively the subepithelial connective tissue takes part in the catarrhal process. The fleshy thickening of the catarrhal mucous membrane was due, in no small measure, to an infiltration of the subepithelial connective tissue with corpuscular elements (fig. 121, *b*). All these cells must be removed before the mucous membrane can be said to have returned entirely to its normal state. Some of them undergo fatty degeneration; others may be taken up by the lymphatics. But weeks may elapse before this is effected; and during the interval, the mucous membrane offers a diminished capacity of resistance to fresh sources of irritation. For the irritability of an organ is proportional to the number of elements susceptible of irritation, which it contains. This is not always sufficiently remembered either by the physician or his patient. The latter is in much the same position as a person whose mucous membranes are predisposed to catarrhal inflammation by a passive hyperæmia. There is always a risk lest the catarrh should return on the slightest provocation, and that in exactly the same part which it has apparently forsaken. The relapse is usually more obstinate than the primary disease; the vulnerability of the mucous membrane, and the consequent risk of a fresh relapse, increases and lasts for a longer time after every recurrence of the inflammation. Every relapse adds to the number of cells in the connective tissue of the mucosa; the epithelium too, and the glandular apparatus, come gradually to take part in the chronic thickening; the mucous membrane becomes hypertrophied. Hypertrophy, viewed in this light, is therefore a result of catarrh; it may also be regarded as a structural cause which predisposes to catarrh, inasmuch as the phenomena which, when taken together, constitute catarrh—*sc.* hyperæmia, swelling, hyper-secretion—have already reached a certain pitch, at which they have become stationary; so that a very trifling provocation suffices to raise them to the level of catarrhal inflammation. (Chronic catarrh.)

§ 356. Let us now consider the anatomical factors of HYPERTROPHY OF THE MUCOUS MEMBRANES one by one.

a. The overgrowth of the CONNECTIVE TISSUE is particularly striking where (as in the gastric mucous membrane) its amount is normally insignificant, where it is a mere cement, holding the closely-packed tubular glands together. The narrow septa between the glandular orifices, as the most superficial locality of this cement, are often the theatre of a very luxuriant overgrowth of young connective tissue; they form villous and lamellar elevations, to a height of one line above the mucous surface, when they may be recognised even with the naked eye. The overgrowth of the connective tissue however—both in its microscopical and naked-eye effects—is thrown very much into the background by the overgrowth of the glands; one is prone to forget that the connective tissue which invests the enlarged glands, which forms the pedicle of a polypus, &c., is itself, in the main, a new formation.

b. The EPITHELIAL LINING of the hypertrophied mucous membrane is quite as continuous as in the healthy state. Hence we may assume that it increases in a horizontal plane, so as to keep pace with the increased area of the mucous membrane itself. It appears, moreover, to adhere more firmly than usual to the connective tissue; for without showing the least breach in its continuity—without *e.g.* the loss of a single columnar cell from the respiratory mucous membrane—it allows the passage, not only of considerable quantities of transuded fluid, but also of great numbers of young cells, which migrate from the deeper parts to the surface, where they mingle with the secretion as pus and mucus-corpuscles.

c. The increase in bulk of the OPEN GLANDS is usually regarded as a functional hypertrophy. Just as the bulk of a muscle increases by exercise, so are the glands supposed to grow in consequence of continued over-secretion. In opposition to this view, I would lay more stress upon the retention of secreted matters, and the passive distension of the glands which ensues. The overgrowth of the subepithelial layer of connective tissue may very plausibly be regarded as a mechanical obstacle to the escape of the secretions. It may compress, narrow, dislocate, occlude the efferent duct, while the body of the gland, especially when situated in the submucous connective tissue, underneath the mucous membrane, may increase in size unchecked. I must not be understood to reduce the glandular hypertrophy to simple dilatation. In the majority of hypertrophied glands we can readily see an elongation or twisting of the tubuli, an increase in the number of acini, as well as a luxuriant cell-growth both within and around the glands. But none the less do I mark, that the tubes and acini of the hypertrophied glands are invariably wider, and contain a larger accumulation of secreted matter than they ought to do; and I look for the stimulus which causes the morbid growth, in a centrifugal pressure of the secretions, which are perhaps unable to escape with due rapidity, owing to the narrowing of the efferent duct, but which, in any case, do not escape fast enough.

§ 357. From this point of view we can readily see how, under certain circumstances, the dilatation may preponderate over the hypertrophy, and how it is that we so often find CYSTOID DEGENERATION associated with glandular hypertrophy, in mucous membranes affected by chronic catarrhal inflammation. The two conditions complicate one another in various ways, giving rise to a series of coarser alterations of the mucous surface, which we may now briefly consider.

What is known as the ÉTAT MAMELONNÉ of the gastric mucous membrane, is due to the fact that the mucous membrane, whose glandular layer is hypertrophied, comes to be too large for the area of its bed, and is therefore thrown into folds with intervening hollows. This plication of the mucous membrane is to some extent—as in the pyloric region—physiological; hence the "état mamelonné" is at first only a quantitative excess. It is only with the aid of the microscope, that we can draw the line between quantitative and qualitative deviations from the normal standard. The dilatation of the hypertrophied tubes, which is usually very striking, serves as a reliable criterion of the morbid nature of the alteration. Higher degrees of the "état mamelonné" pass directly into POLYPOSIS VENTRICULI. We commonly find a number of transitional forms side by side in the same stomach. The folds are subdivided into smaller areas by furrows which cross them at right angles; these are best seen at some distance from the pylorus, about the middle of the stomach; the overgrowth of the glandular layer progresses steadily within these areas. A flattened, roundish tubercle soon projects above the surface. The higher it grows, the more disproportionate is the enlargement of its free extremity; it becomes fungoid and is finally converted into a polypus, with a globular head rather larger than a pea, and a very thin stalk. We occasionally find as many as thirty such polypi upon the mucous membrane of the stomach, with which moreover they vividly contrast by their dark-red hue; from four to six of them are often seated on a common base; next to cancerous products, they cause the greatest and most striking alterations in form, to which the gastric mucous membrane is liable. In their interior we find, besides the dilated tubuli, true cysts scattered here and there; these are filled with a watery fluid or with mucus. The intertubular connective tissue, together with the walls of the tubes themselves, forms septa which take up as much space in proportion to the degenerated tubes, as the septa of an inflated lung in proportion to the alveolar cavities. It was characterised moreover, at least in the cases which I examined, by containing a large number of peculiar, roundly-oval, very lustrous bodies, hardly affected by reagents, whose histological significance I have not yet been able to determine.

§ 358. The "état mamelonné" of the stomach leads on the one hand to "gelatinous" or "cystoid" degeneration of the mucous membrane, on the other, to the formation of mucous polypi. Gelatinous degeneration, which has hitherto been observed only in the mucous membrane of the alimentary canal, comes about as follows: the crypts of *Lieberkühn* are distended with mucus, and converted into retention-cysts as big as a millet-seed; this change is limited to a circumscribed patch, which may, according to *Virchow*, attain the size of half-a-crown. The septa between adjoining cysts become atrophied; the cysts coalesce to form larger cavities; until at last the affected part comes to be mainly made up of mucus, the patch assuming a jelly-like colour and consistency. In mucous membranes which are more scantily provided with open glands, as *e.g.* in the cervix uteri and external os, the affection does not proceed so far as to cause gelatinous degeneration; the distended glands tend rather to project singly above the mucous surface, forming vesicular elevations, or even pendulous cysts (the so-called *ovula Nabothi*); these, in conjunction with the hypertrophied mucosa, which pours out an abundant secretion and is permeated by dilated vessels, constitute the sum-total of structural changes to which the term "chronic catarrh" or "chronic metritis" is applied.

§ 359. Mucous polypi, in the strict sense of the term, are jelly-like tumours, permeated by thin-walled capillaries which give them a reddish hue, and attached to a mucous surface by a more or less distinct pedicle. In outward form they are either smooth and rounded, or lobulated and fissured. When cut into, the surface of section resembles their external surface in colour and consistency; it exhibits in addition, fibrous bands of a milk-white colour, radiating from the root of the polypus to its periphery, as well as mucous cysts of considerable size, which feel hard and elastic before they are cut open. Microscopic examination shows, first, a continuous layer of columnar epithelium investing the outer surface of the polypus. The main bulk of the tumour is made up of hypertrophied glands; we find tubes whose walls frequently bulge outwards to a variable depth, and which terminate in clusters of fully-developed gland-follicles. The tubes are lined with well-formed columnar epithelium; and filled with concentrically laminated masses of viscid mucus. Besides the mucous glands, we find a certain amount of soft connective tissue, rich in cells, which is dense and fibrous only in the pedicle and the bands which radiate from it. The pedicle is chiefly made up of the afferent and efferent vessels; no nerves have hitherto been found in it. We may accordingly take it for granted that mucous polypi originate in a circumscribed hypertrophy of the mucous membrane, which mainly involves its glandular elements. The mucous lining of the nasal fossæ is their favourite seat; next comes the mucous membrane of the uterus. More rarely they spring from the small and great intestines, the larynx and respiratory passages, the female urethra, the external meatus, the sinuses of the upper jaw and frontal bone.

§ 360. Chronic catarrh exerts a very singular influence upon the DUCTLESS GLANDS of the mucous membrane; and this influence is closely connected with the chronicity of the disease. It is only in the tonsils that a true hypertrophy, strictly analogous to the simple hypertrophic alterations considered above, is caused by repeated acute congestion of the pharyngeal mucous membrane. It consists in an equable and uniform overgrowth of all the histological elements of the follicles; of the reticulum, the vessels, the lymph-paths and the cells. The individual follicles may become from three to five times larger than normal. The size and shape of the entire tonsil undergo a corresponding alteration. It forms a globular and often pedunculated tumour, which may project so far into the pharynx as even to interfere with the breathing. Its surface is smooth; even those depressions are effaced which correspond to the orifices of the little crypts round which the follicles are grouped.

These orifices are generally round and open; they are now stopped up and distorted by the swelling.

§ 361. Similar conditions are never met with in the other follicular glands of the alimentary tract. On the other hand we sometimes find, in persons who are especially predisposed, a very singular and important phenomenon: organic inflammations in general, but particularly catarrhal affections of the mucous membranes, causing an enlargement of those lymphatic glands which are nearest the seat of mischief, an enlargement differing from that "acute swelling" which I have already described, by its gradual progress and its obstinacy, and differing from true hypertrophy, by the exclusive proliferation of the corpuscular elements, and the consequent disorganisation of the entire gland; distinguished moreover from both alike, by the enormous size to which the gland may attain. I refer to the scrofulous or cheesy degeneration described in § 203 *et seqq.*, which, when restricted to the mesenteric glands, gives rise to the symptomatic aggregate known as Tabes mesenterica. Sometimes indeed, it occurs in the solitary and agminated follicles of the intestine; but these are so intimately connected with "tuberculous" degeneration of the intestinal mucous membrane, and so constantly associated with it, that it would be inconvenient to treat of them apart. (*See* Tuberculosis of mucous membranes.)

2. *Croupous Inflammation* (*Inflammatio pseudo-membranacea*).

§ 362. Croupous inflammation of a mucous membrane differs from catarrhal inflammation in one essential particular only. The hyperæmia and swelling may be more intense; but it is only in the inflammatory products, that we can discover any *qualitative* difference. These products exhibit the naked-eye characters of a coagulated albuminous substance; they take their name of "fibrin," or "fibrinous exudation," from the chief representative of spontaneously coagulable substances. The material in question is yellowish-white, tough and elastic; when stretched, it is not drawn out into threads, but gives way suddenly and is torn across. On the addition of acetic acid, it clears up and swells like fibrin; its reaction therefore is precisely the opposite of that of mucus, which is rendered opaque and ropy by acetic acid. Morphologically too, the impression conveyed is that of a substance exuded upon the mucous surface, and coagulated at once by contact with the air. For the material in question furnishes a characteristic membranous investment for the mucous membrane ("false membrane") which adheres to the surface as closely as gypsum to a mould. The under surface of the false membrane presents an accurate impression of every irregularity of the mucous surface; should the entire circumference of the mucous tube have been involved, the false membrane forms a tubular cast; should the canal have been of small calibre, the cast is solid and cylindrical; should the disease have been circumscribed, it forms a rounded *plaque*. In thickness, the false membrane varies from a mere bloom-like efflorescence to a rind a line in depth; it sometimes presents a reddish mottling, due to minute extravasations occurring simultaneously with the exudation.

§ 363. All the remaining properties of the false membrane, particularly the histological quality of the seeming fibrin, and the firmness with which the membrane adheres to the mucous surface, vary with its place of origin, and find their explanation in the normal structure of the affected part. Of all the mucous membranes of the body, none is more liable to croupous inflammation than that of the larynx; next in order of frequency come the tracheal and pharyngeal mucous membranes, whose liability is nearly on a par, so that we find laryngeal croup complicated, now with croup of the air-passages, now with that of the pharynx; enabling us to distinguish between a laryngo-tracheal and a pharyngo-laryngeal variety. At the bed-side the former is termed "croup" (Bräune) *par excellence;* the latter, most erroneously, "diphtheria" (diphtheritis, Rachenbräune, pharyngeal croup). The physician has every reason to keep the two varieties apart. In their clinical characters, in the dangers to which they expose the patient's life, and above all as regards their treatment, they differ so essentially, that in spite of their anatomical identity, on which it is my business to insist, I should feel bound to oppose any attempt towards a clinical fusion of the two diseases.

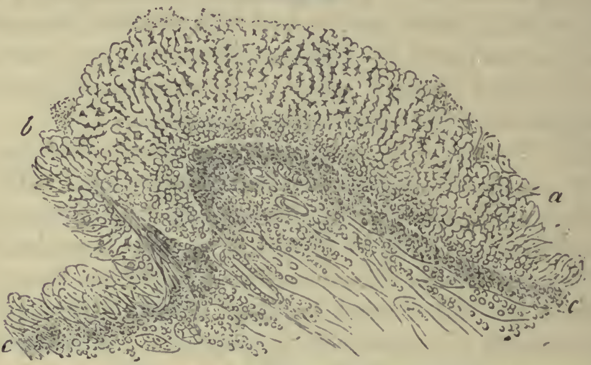
§ 364. We will begin by discussing PHARYNGEAL CROUP, commonly called diphtheria. The morbid process is always insular. At various points of the isthmus faucium, soft palate, and uvula, of the tonsillar surface, palatine arches, and glossoepiglottidean folds—we notice circumscribed spots of a milk-white colour, on an intensely hyperæmic base. The white spot soon rises to a height of half a line at most above the level of the mucous surface, and the false membrane is complete. On attempting to pick it off with a blunt instrument, we find this to be impracticable during its earlier stage; if we use violence, we lacerate the surface and cause bleeding. At a later period, the membrane separates of its own accord; its edges are first of all loosened by a moderate degree of suppuration, and the entire patch is then liberated from its base. The circumscribed catarrh which persists for a time upon the denuded base (often erroneously called an "ulcer"), ceases spontaneously; if not meddled with, it leaves neither loss of substance nor scar. A secondary extension of the false membranes is very rare; they are never known to recur on the same patch, unless previously stripped off before their spontaneous maturation.

§ 365. These striking and important peculiarities are satisfactorily explained by microscopical examination. We learn from this, to our astonishment, that the false membranes do not consist of fibrin. If little shreds of a false membrane are soaked in a weak ammoniacal solution of carmine, then washed and teazed out with needles, we may readily assure ourselves that the naked-eye appearance of coagulated fibrin is produced by cells, and nothing but cells, which have undergone a peculiar degeneration of their protoplasm, and an equally peculiar fusion with one another. But for the reddish dots which indicate the nuclei, we might fairly doubt the corpuscular nature of these angular, lustrous, firmly united flakes. As it is, however, we must consent to the hypothesis of some metamorphosis of the corpuscular elements, concerning whose place in general pathology we can at present only guess. The external appearances may be aptly rendered by the term "glassy swelling," employed by *Weber* to denote amyloid infiltration. It seems certain that the cells contain more solid matter than do normal cells; now if this excess of solid matter were fibrin, we might speak of a "fibrinous degeneration"; inasmuch, however, as we are quite ignorant of its nature, the term "fibrinous degeneration" can only be applied to the naked-eye appearances; even with this limitation, it would involve a tacit assumption which it is better, in my opinion, to avoid.

Let us now examine a vertical section, in order to arrive at some idea concerning the structure and origin of the false membrane. The section (fig. 122) embraces the entire thickness of a false membrane, together with the mucous surface on which it lies.*

We see at a glance that the entire false membrane is really made up of the elements described above. Originally spherical, they have come into contact with one another at various points and have become welded together into a plump network, consisting, in a manner, of "connecting pieces" only, without any trabeculæ. All the more elaborate is the system of crescentic and branching fissures which permeate the false membrane, taking the place of meshes. In certain lights they appear dark,

Fig. 122.



Vertical section through a croupous plaque on the isthmus faucium, with the mucous fold on which it rests. *a—b*. False membrane; *c*. Normal mucous membrane. $\frac{1}{300}$.

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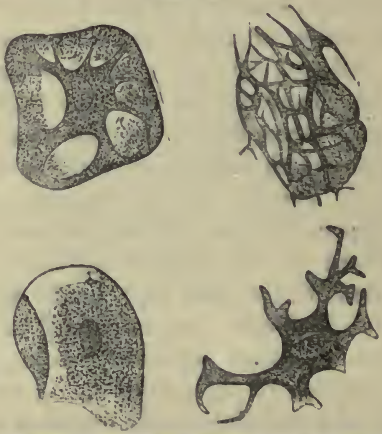
* Deceptive appearances can only be avoided by making the sections exceedingly thin and absolutely vertical. The following is the best method of preparation. The specimen is immersed in a mixture of glycerine and gum-arabic, which must be clear and viscid. After the fluid has had time thoroughly to permeate the specimen, the latter must be taken out and thrown into alcohol. The gum now becomes quite hard, owing to the extraction of the glycerine; and the specimen is quite ready for being cut into sections of any required thinness. On soaking the sections in a watery fluid (say the carmine solution) the gum is dissolved out, and the tissue alone is left.

and so might readily be mistaken for the positive part of the structure; the possibility of error can only be excluded by staining the preparation with carmine. The cells are of variable size; their dimensions increase as they approach the surface; at the extreme periphery of the membrane they are nearly twice as large as lymph-corpuscles; farther inwards they become smaller, the smallest ones lying immediately upon the mucous surface; here too, the degeneration is less marked; they can hardly be distinguished from the normal cells which are still embedded in the parenchyma of the mucous membrane. This gradual transition naturally masks the boundary-line between the surface and the false membrane, though it never quite obliterates it. It proves most undeniably, however, that the false membrane is produced by the secretion of young elements upon the irritated mucous surface, followed by their gradual stiffening, sclerosis, glassy swelling, or whatever term we may choose to apply to their degeneration. Accordingly, the false membrane occupies the precise position which belongs of right to the epithelium; the degeneration in question taking the place of the normal evolution of epithelial elements. What becomes of the original epithelial investment of the affected region? Has it been simply shed, or does it, too, take part in the formation of the false membrane? *E. Wagner* has attempted to solve this problem in a recent and very valuable investigation, and has raised the participation of the epithelium in the morbid process to the rank of a certainty. He describes a very singular metamorphosis of the pavement-cells (fig. 123), in consequence of which the protoplasm disappears at certain points, apparently receding to certain branching lines, where it assumes a homogeneous aspect, and refracts light more highly than ordinary protoplasm. The nucleus disappears; the entire cell being represented only by a network of great delicacy, resembling the antlers of a stag in shape. I believe that I have myself seen this metamorphosis—at least in its earlier stages—along the edges of the false membranes; but I cannot ascribe to it any far-reaching significance as regards their development; the thin stratum of epithelium does not seem to me to possess sufficient resources of its own for the construction of a false membrane. But I am willing to let the future decide on the precise range of *Wagner's* discovery.

§ 366. The intimate connexion between the secreted products and the secreting surface in pharyngeal croup, is the cause of the close adhesion between them at the outset of the disease. When the normal state is re-established, the morbid cell-metamorphosis comes to an end; the cells secreted by the mucous membrane remain unaltered, forming, together with a small quantity of serum which is simultaneously poured out, a thin layer of purulent fluid; and this of itself involves the detachment of the false membrane.

Notwithstanding the superficial character of pharyngeal croup, it is a very dangerous affection, owing partly to the constitutional disturbance which attends it, partly to the risk of laryngeal complications; the pharyngeal angina being associated with a laryngeal angina, due to a swelling of the submucous connective tissue, which may assume alarming proportions.

FIG. 123.



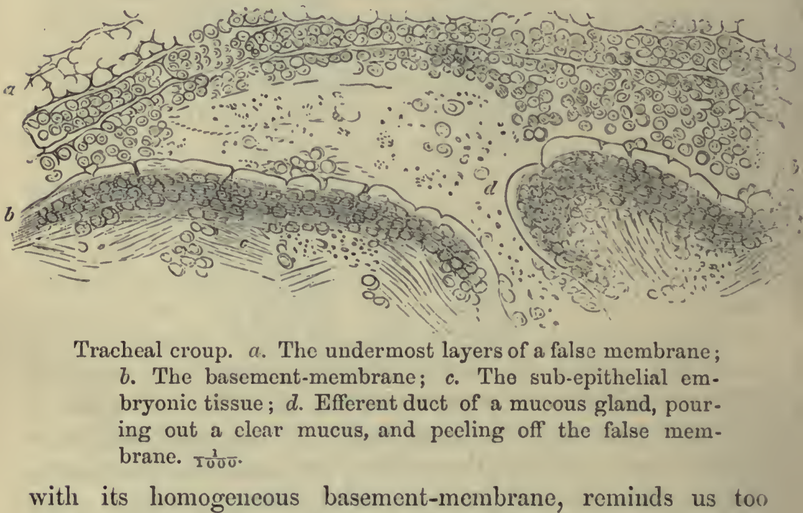
Fibrinous degeneration of pavement-cells (after *E. Wagner*).

§ 367. Croupous inflammation of the LARYNX and TRACHEA presents us with a serial succession of simple catarrh and pseudomembranous exudation. Even in its catarrhal stage it is capable of giving rise to the familiar group of symptoms in their highest intensity—nay, even to death itself. The laryngeal mucous membrane is acutely inflamed, and proportionately swollen; it secretes a viscid and tenacious mucus, rich in cells; this forms a thick, adhesive, yellowish layer, contracting the already narrow chink of the glottis to such a degree, that we need hardly recur to the assumption of reflex spasm of the glottis to account for death by apnœa. Accordingly, a number of physicians have gone so far as to deny the occurrence of a fibrinous exudation altogether. We must not fall into this error. The development of a false membrane is connected in the closest manner with the catarrhal state, and constitutes the anatomical acme of the morbid process. We often find the two conditions side by side, a layer of catarrhal secretion being interspersed here and there with patches of fibrinous exudation. Acetic acid enables us to distinguish at once between the muco-purulent and the fibrinous elements; no uncertainty is therefore possible upon this point.

Histological examination of the false membrane shows, first of all, that here too, corpuscular elements predominate. These are far more easily recognisable than in the pharyngeal false membrane; they resemble for the most part, the cells of ordinary embryonic tissue. In vertical sections (fig. 124) however, we find that these embryonic cells are not the only constituents of the false membrane. It presents an exquisitely laminated structure, the corpuscular layers alternating at tolerably regular intervals with layers of fibrin; these alternate layers recurring from one to ten times, in proportion to the thickness of the membrane. Whether I am justified in calling the alternate layers "fibrinous" or not, must remain open for the present. I call them so from the first impression which their configuration makes upon the observer's mind, and with the reservation that I mean no more by the word than a fluid albuminous substance, which has coagulated after transudation on exposure to the air. The substance in question is lustrous and homogeneous; I have not been able to resolve it into cells, like those of the pharyngeal false membrane; it forms thin plates with upward and downward processes which penetrate into the interstices between the contiguous cells, forming by their anastomoses a beautiful network, whose meshes correspond very nearly to the individual cells (*a*). Under such circumstances, I think we may fairly infer, that a fluid, in which a large number of cells are suspended, and which holds the "fibrinoid" substance in solution, has been secreted by the mucous surface; further, that the coagulation of this fluid has fixed the cells in their original position, while the extension of the coagulation to the lacunar interstices between the spheroidal bodies of the cells, has given rise to the appearance of a network.

Hence the difficulty of accounting for the place and mode of origin of these cells. The epithelium has long since disappeared; it must have been stripped off at the very outset of the process by the development of the false membrane, just as in the pharynx; admitting the possibility of a fibrinous degeneration, such as is described by *Wagner* (*see* § 365), the uppermost stratum of the network might perhaps be regarded as consisting of the bodies of the columnar epithelia, after their branching and stiffening; this view would lead us, however, to ascribe a different origin to the different layers of the network; a lack of uniformity which would be most undesirable. And yet the mucous membrane of the trachea, stripped of its epithelium, with its homogeneous basement-membrane, reminds us too forcibly of the "open palm" of Charles VII.* not to make the lacuna in our interpretation very sensible. Our only hope lies

Fig. 124.



Tracheal croup. *a.* The undermost layers of a false membrane; *b.* The basement-membrane; *c.* The sub-epithelial embryonic tissue; *d.* Efferent duct of a mucous gland, pouring out a clear mucus, and peeling off the false membrane. $\frac{1}{1000}$.

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*In *Schiller's* Jungfrau von Orleans (Act i. sc. 3) King Charles is made to exclaim, despairingly:

> "Kann ich Armeen aus der Erde stampfen,
> Wächst mir ein Kornfeld in der flachen Hand?"

"Can I raise armies from the earth with a stamp of my foot, or grow a cornfield in my open palm?"

For this reference I am indebted to the kindness of Professor Buchheim.—Tr.

in the highest magnifying powers. With one of *Hartnack's* immersion-lenses, I have succeeded in making out that the "homogeneous" basement-membrane is not really homogeneous, but perforated by a large number of very fine pores. Through these pores the cells, of which there is usually a certain quantity stored up between the basement-membrane and the elastic layers, make their way to the surface. The apertures indeed are small; but is there any aperture so small as not to allow the body of a young embryonic cell to slip through it? Those who, from personal observation, are familiar with the amœboid movements of these cells, will agree with me in answering this query in the negative; they will also admit that the "homogeneous" basement-membrane presents no obstacle to their migration.

§ 368. The presence of this basement-membrane underlies, moreover, another important peculiarity of the croupous membranes of the trachea, *sc.* that from the very first they adhere less closely to the mucous surface than the false membranes of the pharynx. Not only does the boundary-line between mucous membrane and false membrane, between the secreting surface and the secreted products remain clear and distinct throughout, but the smoothness of the surface gives little chance of any lasting union ever being brought about between the two. Consider moreover the activity of the mucous follicles; the free escape of their secretions is often hindered by the superjacent false membrane, which they accordingly detach by accumulating underneath it (fig. 124). The upshot of all these conditions is the ease with which false membranes of the trachea may be peeled off, a property on which all our therapeutic measures, inadequate as they are, repose. Indeed the separation of the false membrane not unfrequently proves the immediate cause of death; the membrane, wholly or partially detached, becoming rolled up and completely blocking up the tube. The membranes in tracheal croup may undergo softening as well as separation. A gelatinous transformation of the network, together with a fatty-granular disintegration of the embedded cells, are the chief factors in this process. Some observers have detected fungoid vegetations in the softened pulp, and have accordingly ascribed more of a putrid character to this liquefaction. The naked-eye appearances justify us in calling it a true "melting," inasmuch as the membrane does not merely become fluid at its edges, but exhibits thinning and perforation at various points in its continuity as well, the perforations ultimately becoming confluent. I have only seen one case of this kind; I recollect that the fluid products of softening yielded a precipitate of mucin on the addition of acetic acid; and this led me to speak of a "mucoid" softening of the false membrane.

§ 369. Having discussed the croupous process as it presents itself in the pharynx and trachea, we may conclude with a few words about laryngeal croup. A croupous inflammation, confined, throughout its entire course, to the larynx, is of rare occurrence; nevertheless, the laryngeal is the most common variety of croup, inasmuch as it nearly always complicates croup of the air-passages, and may also complicate that of the pharynx. The characteristic features in the morbid anatomy of laryngeal croup are due to the fact that the mucous lining of the larynx agrees in its structure, partly with that of the pharynx, partly with that of the trachea. Both surfaces of the epiglottis, and the true vocal chords, are coated with a laminated pavement-epithelium, which is not marked off from the connective tissue by any homogeneous basement-membrane. Hence the false membranes adhere more firmly to these, than to any other points in the interior of the larynx. How often do we find, in making a post-mortem examination, that the tracheal false membrane, continuous with that of the laryngeal funnel, is quite loose as far up as the rima glottidis, where it is firmly attached; and we feel sure that its spontaneous detachment at this point would have required a very long time for its accomplishment. Yet it is just the true chords which are especially liable to become inflamed, while the ventricle of Morgagni, for instance, is hardly ever affected. From an etiological point of view it seems to me very important to lay stress upon the preference which the disease exhibits for the prominent parts of the mucous membrane, while its recesses are, for the most part, intact. It is as though the pharynx had been lightly brushed over with some corrosive agent, or as though some irritant gas had been retained for a short while in the upper part of the respiratory passages.

3. *Diphtheritic Inflammation.*

§ 370. After the exclusion of what is commonly known as "pharyngeal diphtheria" from the domain of diphtheritic inflammation, the extent of the latter remains comparatively limited. We have already touched upon the essential features of the process, in our account of the "diphtheritic pock" (§ 298). It consists of an infiltration of newly-formed cells into the subepithelial connective tissue, as contrasted with the entire mucosa; an infiltration so abundant as to compress the vessels, and to arrest both circulation and nutrition. Inasmuch as a certain amount of corpuscular infiltration of the subepithelial connective tissue occurs in connexion with every catarrh, as well as with the croupous form of inflammation, diphtheria may be regarded as merely a quantitative increase or excess of this morbid proliferation; true diphtheria having no claim to be regarded as a specific process in the same degree as croup. To the naked eye, it presents certain characters which have led to its being contrasted with the "Inflammatio pseudo-membranacea" as an "Inflammatio membranacea"; I refer to the formation of a tough, felted membrane of a greyish-white colour, often mottled with shades of red and green (due to blood-pigment), raised to the height of about half a line above the level of the mucous surface, penetrating downwards into its substance to the same extent, and intimately blended with it. This membrane is not a deposit upon, or a secretion from the mucous surface; it is the mucous membrane itself, so much of it at least as has been at once tumefied and deprived of blood by the excessive corpuscular infiltration. This condition has been compared, not inaptly, to mortification caused by a chemical irritant, to a corrosion, and the diphtheritic membrane has been called a "diphtheritic slough"; the membrane is indeed a *caput mortuum*, it cannot enter upon any changes save putrefaction and decomposition; we have only to inquire how it is set free from its close organic union with the mucous membrane, and cast off. Simple inspection is enough to show us that a sharp line of demarcation separates the living tissue from the dead; but a number of connective-tissue fibres, blood-vessels, nerves, and elastic fibres, pass from the living into the dead parts; and these must all give way before separation can occur. The means at the disposal of the organism are inflammation and suppuration. We call this form of inflammation "reactive," meaning thereby that it is supposed to respond, as it were, to the irritation exercised on the surrounding mucous membrane by the diphtheritic slough; some portion, however, of the hyperæmia may be interpreted as a collateral fluxion, occurring in harmony with statical laws (*i.e.* of a passive, not an active kind). The pus collects between the slough and the healthy tissue; the former begins to separate at its edges or at its centre, according as the fibrous bridges alluded to above, melt and give way in the former or the latter order. When the separation is complete, an ulcer is left, which tends speedily to cicatrise; a recrudescence of the morbid process not unfrequently occurs, a new slough is formed, a renewed necessity arises for a sequestrating suppuration, the resulting loss of substance being far more considerable than it was in the first instance. The scars which are ultimately left are very prone to contract, so that the risk of a subsequent stricture of the mucous tube (particularly of the large intestine after dysentery) is directly proportionate to the extent of the previous ulceration.

§ 371. It is worthy of note that diphtheria affects such mucous membranes as are already in a state of violent catarrhal inflammation, and whose surface is at the same time in permanent contact with putrescent, decomposing substances. In dysentery, which begins as a simple catarrh of the greater bowel, accompanied by excessive spasmodic contractions of its muscular coat, the diphtheritic process primarily affects the free borders of the mucous folds over the *tæniæ longitudinales* and the *plicæ sigmoideæ;* also those natural flexures of the intestinal tube where most resistance is offered to the passage of the fæces, *sc.* three successive points in the sigmoid flexure, the cœcum, the hepatic and splenic flexures of the colon. Now the circumstance, that at these points the inflamed mucous membrane is longest and most closely in contact with putrid matters, must surely aid in the localisation of the diphtheritic process. In much the same way, diphtheria complicates those catarrhal affections of the urinary passages which are due to retention. Whether the retention be caused by stricture of the urethra, by enlarged prostate, by paralysis of the detrusor muscle, &c., the stagnant urine becomes decomposed, and sets up a catarrh passing into diphtheria of the mucous surface. Contact with putrid matter also contributes to cause those diphtheritic lesions which occur, not on a catarrhal, but on a denuded surface. I refer to diphtheria of the womb and vagina immediately after parturition, when the shedding of the decidua has left the uterine parenchyma unprotected and raw, like an amputated stump; I refer to the diphtheria which occasionally complicates the second stage of Asiatic cholera, after the violent catarrh of the first stage has stripped the mucous membrane of all its epithelium, and left it a prey, in this its "flayed" condition, to the direct influence of the intestinal contents; finally I refer—although this has really nothing to do with the mucous tract—to that diphtheria of wounds which is known as hospital gangrene.

On the other hand, it cannot be denied that the element of putridity may also reside within the organism; that there is a state of the fluids in the individual which predisposes him to become affected by diphtheritic inflammations—or, to speak more accurately—which predisposes any inflammation, otherwise excited, to take on a diphtheritic character. Many diphtheritic inflammations of the pharynx and alimentary canal, complicating the last stages of maladies which profoundly affect nutrition, may be thus explained. In conclusion, I must not omit all reference to a statement which has over and over again been repeated (*Letzerich*), to the effect that diphtheritic inflammation is due to the germination of a fungus upon ulcerated and mucous surfaces. Although I am by no means hostile to this view, I do not regard it as well enough established to warrant my bestowing any lengthy notice upon it on the present occasion.

b. HÆMORRHAGE.

§ 372. I am by no means sure that my grouping the various matters which I propose to discuss in the present chapter, under the common head of "Hæmorrhage," will meet with universal approval. The reader's attention has already been called (§§ 353 and 240) to the facilities afforded by the arrangement of the capillaries in the gastro-intestinal mucous membrane, for the occurrence of hyperæmia and hæmorrhage. In the more lively contractions of the muscular coat, which accompany catarrhs even of trifling intensity, but which are especially characteristic of their dysenteric form, we saw a reason for the extravasation of blood either into the parenchyma of the mucous membrane, or upon its surface. Now on the gastric and duodenal mucous membrane there occur a series of conditions, characterised by loss of substance, which may very plausibly be referred to antecedent parenchymatous hæmorrhages—to hæmorrhagic infarctions of the mucous membrane. This view is generally adopted to explain HÆMORRHAGIC EROSIONS. Under this term we understand certain sharply-circumscribed, circular defects of the mucous surface, no larger than a pin's head, which commonly occur in great numbers, their favourite seat being on the free borders of the mucous folds in the pyloric region. The frequency of hæmorrhagic infiltrations of the same size and shape, existing side by side with the erosions, raises the probability of their originating in this way to a certainty. Moreover there is usually a history of attempts at vomiting, to account for the presence of the hæmorrhagic extravasations; so that we may fairly assume the sequence of phenomena to have been something like this: the act of vomiting, by temporarily arresting the return of blood, causes minute extravasations from the superficial venous radicles of the gastric mucous membrane; these occur on the free borders of the folds, the extreme parts of the congested area, where the blood-pressure must attain its maximum intensity. The extravasated blood-corpuscles infiltrate a circumscribed patch of the mucous membrane to such an extent as to compress the capillaries, thus putting a stop to circulation and nutrition. The hæmorrhagic infarction becomes a *caput mortuum*, its organic union with the healthy mucous membrane is at an end, and its actual detachment becomes merely a question of time. When we reflect how easily the gastric juice can dissolve such dead parts as these hæmorrhagic infarctions, we shall readily understand how it comes about that a very few hours after the bleeding has occurred, we should find, in place of the infarction, that sharply-defined and regular loss of substance, to which *Cruveilhier* gave the name of "érosion hémorrhagique."

§ 373. I agree with many other observers in assigning a similar mode of origin to the simple (chronic, circular, perforating) ULCER OF THE STOMACH. On December 4th, 1865, a man was admitted into the surgical wards at Bonn with a strangulated inguinal hernia. He had been vomiting continually from

5 A.M. Unsuccessful attempts had been made to reduce the hernia. At 7 P.M. operation, followed by relief. On the evening of Dec. 5, an enema was followed by a copious stool of a dark-brown colour; on the 6th another stool was passed, consisting of black, altered blood. During the night between the 6th and 7th, nausea and retching; on the morning of the 7th vomiting of lumps, streaked at first with bile, and later with blood; this frequently recurred throughout the day, and lasted with brief intermissions until the patient's death at 9 P.M. At the post-mortem examination, performed one hour after death, the stomach presented, besides several hæmorrhagic infarctions of smaller dimensions, two circular foci of equal size, symmetrically disposed on either side of the middle line of the lesser curvature; of these, one was a perfect example of a simple ulcer, while the other presented the appearance of a hæmorrhagic infarction of the gastric mucous membrane of corresponding size.

For prolix hypotheses concerning the possible or probable mode of origin of gastric ulcer, which would outrun the limits of this manual, I substitute the above plain record of a case with a post-mortem. And this I do, partly in order to substantiate the view which I have adopted, partly also to point out how very unstable all those theoretical arguments must be, seeing that the results of a single post-mortem are still of such importance in the settlement of the question.

§ 374. The simple ulcer accordingly originates in a hæmorrhagic infarction. This involves the entire thickness of the mucous membrane. In fine sections through the above specimen, I was everywhere able to demonstrate the bodies of the tubular glands bathed in blood-corpuscles, as though embedded in the clot. The solution and removal (digestion) of the infarction by the gastric juice, leaves a corresponding loss of substance; the simple ulcer is complete. It may get bigger, it may go on to the dreaded issue of perforation; or it may, on the other hand, contract and cicatrise; I repeat however, that it is complete in all essential particulars the moment the infarction is detached.

First among its essential features is its circular outline. I ought to say, the circular outline of its base, for its shape as a whole is that of a very shallow cone, whose base is directed towards the surface of the mucous membrane, while its apex is excentric in position, penetrating into one of the deeper layers of the gastric wall. If we would know the cause of this conical or funnel shape, we must go back to the hæmorrhagic infarction as the starting-point of the lesion. Like every other hæmorrhagic infarction (of the lungs, kidneys, &c.), this is limited to the area of distribution of a single vessel; now the vascular territories of the stomach possess the form of shallow, obliquely truncated cones, whose apices are directed upwards in the upper half of the organ, downwards in its lower half. This explains how it is that the deepest point of the funnel-shaped crater is situated, not under the centre of the hole in the mucous membrane, but nearer its upper or its lower edge as the case may be.

Another, not less characteristic feature of the simple ulcer, is the exceeding sharpness of its edge, and the absence of any raised border. The mucous membrane looks as though a hole had been cut in it with a punch. The submucous tissue is as clean and white as though it had been carefully dissected; and if the ulcer perforates it also, the perforation is circular and sharply cut, showing the muscular coat with its transverse bundles as if dissected out. It would seem as though the formative reaction at the base and edges of the ulcer were quite insignificant; moreover, that the digestive solution followed so closely upon the heels of the plastic infiltration, as to prevent our ever getting a glimpse of the latter at all. The very chronic character of the process, which often drags through more than one decennium, is in favour of the former assumption; while the latter is supported by the fact that the simple ulcer is only found in the stomach and the upper part of the duodenum, *i.e.* only in that part of the alimentary canal where its contents are acid, and where the solution of albuminous substances takes place most rapidly.

§ 375. As regards the further progress of the simple ulcer, the possibility of its cicatrisation has already been referred to. The smaller and more recent the lesion, the sooner may the formation of the "stellate cicatrix" be expected to occur; *i.e.* of that minute, white, flattened scar, which replaces a loss of substance perhaps ten times as large as itself, and which must necessarily contract and pucker the neighbouring mucous membrane. Ulcers of larger size may also become cicatrised, but this does not commonly occur; when it does, it may lead to such extensive contractions of the stomach at its middle part, as to subject the patient to a fresh series of troubles.

On the other hand, the gradual extension of the original ulcer exposes the patient's life to three sets of risks. For when the ulcer continues to increase in depth slowly but unceasingly—

1. It may open into a large vessel, and so cause fatal bleeding into the stomach. Such an issue is most frequent in the case of those ulcers which are situated on the posterior aspect of the stomach, just over the course of the splenic artery; sometimes, however, it is the trunk originally supplying the affected area which is laid open *per diabrosin;* the hæmorrhage then occurring from a branch of the coronary or gastro-epiploic arteries.

2. It may open into the peritoneal cavity. This usually occurs by a circular hole of fair size, which can hardly be produced otherwise than by necrosis of the base of the ulcer, and detachment of the necrosed part. This accident is most common in the case of duodenal ulcers; next in order of frequency come ulcers on the anterior wall of the stomach, inasmuch as during the various movements and changes of place which the organ undergoes, its anterior surface moves up and down over a considerable area of the opposite peritoneal surface, a circumstance very unfavourable, nay, antagonistic to any prophylactic adhesion. The possibility of such conservative peritonitis is clearly shown by ulcers situated on the posterior wall of the stomach and in the pyloric region; these are almost invariably found to have contracted adhesions to neighbouring viscera, such as the liver, pancreas, spleen, &c., before the occurrence of perforation. This wards off the risk of a rapidly fatal peritonitis; the result is one which we, as physicians, would endeavour to compass if we could. We must not shut our eyes to the fact, however, that this very bridging-over of the interval between two layers of peritoneum opens a new field for the destructive activity of the ulcer, which may proceed—

3. To burrow into a neighbouring organ and destroy it layer by layer. The spleen and the left lobe of the liver are most liable to be thus invaded; and as the destructive process advances with greater ease in their soft parenchyma, than in the walls of the stomach and the connective tissue of the adhesion, they

speedily become hollowed out into large cavities, which communicate with the stomach by a narrow opening. More rarely does the ulcer burrow into the head of the pancreas; rarest of all is adhesion between the stomach and colon, whereby these divisions of the alimentary canal are made to communicate, giving rise to the symptoms of lienteric diarrhœa. I have seen a case in which adhesion and subsequent perforation united the pylorus with the gall-bladder; gallstones being subsequently formed and discharged by vomiting.

c. SPECIFIC INFLAMMATION.

1. *Typhus.**

§ 376. The typhous process, in by far the most frequent mode of its occurrence, ileotyphus (*typhus abdominalis*) is associated with certain changes in the mucous membrane of the intestine, which undeniably possess special anatomical peculiarities. Like those of syphilitic gummata, leprosy, and tubercle, these special characteristics are manifested rather in the coarser anatomy, than in the finer structure, of the morbid products. The attention of physicians has only been directed to them since the third decade of the present century. They were originally described as "inflammation of Peyer's patches"; then *Heusinger* pointed out their similarity to medullary cancer; *Rokitanski* compared the aspect and consistency of the altered patches to the cerebral medulla of young children, and introduced the term "medullary infiltration," which is still in use, to designate their appearance when mature.

Concerning the relation of the intestinal and other anatomical changes (splenic enlargement) to the constitutional disorder, great differences of opinion still exist. The Vienna school considered the changes in the bowel as a mode of eliminating the peccant matters from the blood; at the present day, we have only two alternative opinions from which to choose; we may regard the bowel-lesions as standing in the relation of an exanthem towards the constitutional disorder, or we may ascribe them to the local action of the typhoid poison, inasmuch as they are produced in those very organs which are probably, according to recent investigations (enteric fever from drinking-water), the channels through which the poison is introduced into the system.

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* For reasons alluded to in § 112, *note*, I have kept the generic term "Typhus" employed by the author. It is self-evident that the chapter refers solely to abdominal typhus or enteric fever.—TR.

§ 377. Several stages have been distinguished in the course of abdominal typhus; the catarrhal stage, the stage of medullary infiltration, the stage of degeneration, and that of ulceration. We will retain these divisions, premising however, that the general catarrh of the alimentary tract which ushers in the process, may continue, without undergoing any marked abatement, until the final stage. Strictly therefore, the division into stages is only applicable to the special alterations in the lymphatic follicles, on which indeed the attention of the anatomist is concentrated from an early period. During the catarrhal stage (which seldom comes under observation), all the Peyer's patches, and the solitary follicles of the small and great intestine, become swollen in the manner described in § 350. The greyish, pearly nodule, surrounded by its close web of vessels, is the acme of the process in this direction; thereupon, the swelling for the most part subsides entirely, particularly in the solitary glands; here and there, especially in Peyer's patches, the character of the swelling undergoes a change, without the occurrence of suppuration and expulsion of the follicles; the latter passing into the state of "medullary infiltration."

This "medullary infiltration" is mainly distinguished, on the one hand by an enlargement of the follicle, which may attain even six times its normal size, on the other by an extension of the morbid process to the perifollicular connective tissue. The follicles which make up a Peyer's patch, coalesce with the interstitial connective tissue to form a soft, rose-coloured, seemingly homogeneous mass, which closely resembles the medullary substance of the fœtal brain; the entire patch forms a flattened elevation, about two lines in height, of an elongated oval outline; it is marked off from the surrounding mucous membrane by a precipitous border. The solitary follicles are converted by the infiltration into marrowy nodules, from two to four lines in diameter; it is in these, that the extension of the morbid process to the mucosa is most strikingly apparent; since the greater part of the nodule is obviously made up, not of the follicle itself, but of the mucous membrane which covers it.

§ 378. What light does the microscope throw upon this "medullary infiltration"? Does it enable us to detect any typical tissue-change, which, independently in some measure of pre-existing structure, is able to generate "typhous" products wherever connective tissue or lymphatic elements may happen to exist? May we speak of a "typhous" product in the same sense as of a cancerous, sarcomatous, or syphilitic product? I feel myself entitled to the credit of having done my best to penetrate into the anatomical essence of the typhoid process, with the aid of the most recent methods of investigation. The results, however, have not proved equal to my expectations. Other observers have described corpuscular and nuclear proliferation as the only demonstrable appearances. I will venture a step farther, and call attention to some points which, in the general absence of "peculiarities," seem to be worthy of being put on record. First then, let me refer to the enormous dilatation of the capillaries and arterioles in the parts affected with medullary infiltration. The double contour of their walls is represented merely by a sharp line of demarcation between the parenchyma and the blood; the blood seems occasionally to have become quite stagnant, if we may judge by the appearance of the colourless corpuscles, which, just as in cases of slow coagulation, have become aggregated into little clusters, occupying, without any admixture of red ones, the whole interior of a capillary vessel for short portions of its course. Notwithstanding this however, ecchymoses are rare; probably because the elastic reaction of the proliferated parenchyma is too powerful to allow of their production.

As regards the morbid products themselves, I have already pointed out (in § 112) that the process does not consist merely of a numerical multiplication of elementary parts, as in catarrhal inflammation, but that in addition to this numerical increase, which is undoubtedly very considerable, there is an increase in the size of the individual elements, a tendency towards the production of a specific "typhous" cell. The individual evolution appears indeed to culminate in the production of this "typhous" cell, a structure which differs from the simple lymph-corpuscle, by containing a larger proportionate amount of protoplasm. The protoplasm of a lymph-corpuscle barely equals the contained nucleus in amount; whereas in the "typhous" cell, it always takes up as much, on an average even more space than the nucleus. The "typhous" cell represents the first step towards, as it were a foreshadowing of, epithelial differentiation: it would seem, however, as though this augmentation of the protoplasm lacked the solidity and durability of epithelial development, inasmuch as the "typhous" cells remain but a short while at their acme, and speedily fall a prey to necrobiotic change.

Finally, as regards the peculiar rosy, homogeneous tint of the entire mass, it is explained by the dark-red hue of the turgid capillary network being toned down to a uniform flesh-colour, by the homogeneous medium through which we see it.

§ 379. The anatomical alterations culminate in medullary infiltration. This is followed by retrograde metamorphoses, which may set in in diverse ways. The great majority of the infiltrated patches gradually return to their normal state by a "colliquative softening." The "typhous" cells become disintegrated into oily *débris*, which are absorbed as chyle. Thereupon the swelling disappears, the follicles being the first to subside; the Peyer's patch presents a reticulated aspect (*surface réticulée*) owing to the collapse of the follicles; the little hollows which correspond to them forming the meshes of a network, whose trabeculæ are represented by the interstitial connective tissue which still continues infiltrated. When the latter is also freed from the infiltrated products, nothing more remains to be done save a gradual restitution of the lost parts, which appears to begin at once.

§ 380. But this "colliquative softening" is not the only way in which the morbid products may be got rid of; another and a more severe issue, is "sloughing" of the deposit. We found that nearly all the lymphatic structures in the wall of the alimentary canal were implicated during the catarrhal stage; we found a marked limitation and concentration of the process in the stage of medullary infiltration; now in the stage of sloughing, a further and much the most striking reduction in the extent of the morbid process, takes place. Small portions of single Peyerian patches, portions varying from a lentil to a size of from three-fourths to five-fourths of an inch, with here and there a solitary gland, assume a yellowish-white, opaque tint instead of their former reddish and translucent aspect; they are detached from the surrounding tissue by a sharp line of demarcation, and then pass into a state of cheesy necrosis. When once this has occurred, recovery can only take place by expulsion of the necrosed parts and consequent ulceration. An increased degree of congestion at the edges of the slough, is followed by suppuration, and detachment of the dead part; the latter continues, however, to hang on for a long time to the base or edges of the ulcer, and acquires a yellow, green, or brown tint, by contact with and imbibition of bile-pigment. It finally comes away in shreds, leaving an ulcer whose size is determined by that of the slough, and whose floor is usually composed of the deepest layer of the submucous connective tissue. In severe cases the ulcer penetrates still more deeply, and the expulsion of the sequestrum coincides with perforation into the peritoneal cavity. In such cases we may infer that the infiltration extended from the first, not only through the entire thickness of the submucous tissue, but also through the interstitial connective tissue of the muscular coat, to the subserous and serous layers.

The healing of these typhoid ulcers follows at once upon the sequestrating inflammation. No sooner is the slough thrown off, than a small quantity of embryonic tissue springs up on the floor of the ulcer; the precipitous abruptness of its edges is undermined by a colliquative softening; the collapsed border overhangs a portion of the denuded floor, to which it speedily becomes attached by cicatricial tissue; the central part, which is still naked, comes at a later period to form a smooth, lustrous surface, with pigmented edges, on which neither villi, glands, nor any of the other component elements of a mucous membrane, are ever regenerated. By transmitted light, these patches appear thin and transparent; this is due to the absence of a mucous layer.

As regards the intestinal hæmorrhages which occasionally complicate abdominal typhus, it may be remarked that the frequent, trifling, and harmless ones, occur by diapedesis from the over-congested edges of the ulcers; the more severe bleedings, from those larger vessels, which served at one time to convey blood to the necrosed tissues, and which are now liable to be torn, perhaps in consequence of premature detachment of the sequestra by passing fæcal masses.

§ 381. So much for the morbid changes in the mucous membrane. In constant association with them, we find an affection of those mesenteric glands which draw their lymph from the infiltrated portions of the bowel. As the ileum is always most intensely affected for about twelve inches above the ileo-cœcal valve, it is here that we may expect to find the most perfect examples of the morbid changes in the lymphatic glands. In their histological characters these faithfully reproduce the primary disorder. A moderate degree of catarrhal swelling is followed by a medullary intumescence of colossal proportions, nearly approaching those of scrofulous enlargement. It becomes impossible to distinguish the boundary-line between cortical and medullary substance with the naked eye. The microscope shows that the follicles and their prolongations into the medulla (the lymphatic nodules and trabeculæ) are the chief seat of morbid change, while the lymph-sinuses, and especially the connective tissue, are infiltrated with "typhous" elements to only a moderate extent. Here—*i.e.* in the lymphatic nodules, of which from fifteen to twenty may, as we know, be counted in a longitudinal section through a gland of average size—we meet, first, with that inordinate dilatation of the capillary network which seems to me to be the most characteristic feature of the medullary condition. Side by side with this dilatation, we may often note an obvious "plugging" of many capillary loops, and even of some of the larger vessels, with a dark, granular matter, concerning whose nature I am still in doubt. Further, the condition of the adenoid reticulum is very singular. All its trabeculæ are from three to four times thicker than usual; the nodal points are especially swollen, the nuclei themselves vesicular; the old anastomotic network of corpuscles has obviously returned to life, the shrunken cells have grown plump by the absorption of pabulum, the nuclei are ready to resume their function as cytoblasts. The continuity of the network is already interrupted at many points; the resulting gaps being occupied by globular aggregations of cells. The proliferation is mainly fissiparous, though the endogenous mode is also not unfrequent. The edges of the lymphatic trabeculæ—the brink of the stream of lymph—are often so thickly studded with mother-cells, that these even outnumber the ordinary lymph-corpuscles. Here too, the process ultimately tends to the development of the maximum number of "typhous" cells. The acme once reached, every space in the interior of the gland which is not pre-occupied by the vessels—among others the lymph-path itself—is gorged with these elements. It is impossible, even with the best injecting fluids, to fill the lymph-path of the infiltrated gland; indeed injection serves to show the stage at which the process has arrived. Here too, the law which regulates all other progressive changes in the lymphatic glands (scrofulosis, cancer, &c.) is found to hold good, viz. that the swelling should begin at the periphery of the gland, in those parts of it which are nearest the seat of primary disease from which the infecting lymph is drawn, spreading gradually from thence to the entire parenchyma. The degenerative changes follow the same order. These almost always consist of a "colliquative softening," with complete fatty degeneration of all the "typhous" cells. Inasmuch, however, as all the lymph-corpuscles and connective-tissue corpuscles, *i.e.* nearly all the normal corpuscular elements of the gland, have been converted into "typhous" matter, we may readily understand how it comes that hardly anything is left beyond the capsule and the blood-vessels. The uttermost limits of collapse are reached; the antecedent congestion has already given rise to distinct extravasations with subsequent pigmentation in the capsule, so that a slaty discoloration figures among the characteristic features of the shrunken "typhous" gland.

The occurrence of cheesy necrosis at one or more points of a mesenteric gland in abdominal typhus, must be regarded as a rare phenomenon. *Virchow* has repeatedly called attention to its possibility. The cheesy slough is then detached by a suppurative inflammation, and a minute abscess results. This may burst into the peritoneal cavity; hence the risk of peritonitis; on the other hand, the pus may become inspissated, and finally calcareous. The earthy nodule is invested with a capsule of connective tissue, like any other foreign body, and the process is at an end.

§ 382. All the remaining forms of swelling, productive activity, &c., which are associated with the "typhous" process, are found, upon analysis, to consist of the same series of progressive and retrogressive changes. We know least about the fine anatomy of the splenic enlargement; the relative proportion of congestion to morbid growth, has not yet been ascertained for the different stages of the disease. True medullary infiltration has been detected here and there in the Malpighian corpuscles. The "typhous" deposits which are occasionally met with in the serous membranes, the liver, and the kidneys, are precisely analogous to the changes in the intestinal mucous membrane. The alterations in the fibres of voluntary muscle (*Zenker*) will be fully described hereafter (§ 756).

2. *Tuberculosis.*

§ 383. Before beginning the study of tuberculosis as it occurs in mucous membranes, we must learn to discriminate carefully between tuberculous disease of mucous membranes, and those diseases of the mucous membranes which occur in tuberculous patients. It is only in a few instances that the development and decay of tubercles constitute the sum-total of the morbid changes; in a somewhat larger proportion of cases, they form the leading feature of the disease; as a general rule however, the actual growth of tubercles occupies a relatively subordinate position, in comparison with the non-tubercular alterations, serving as a sort of excitant or guiding impulse—as a standing witness to the specific and incurable nature of the malady.

§ 384. TUBERCULOSIS OF THE URO-GENITAL MUCOUS MEMBRANE affords the best example of the changes which tuberculosis *per se* is capable of effecting—of the disturbances which may be ascribed exclusively to it. The tuberculous ulcer of the urinary bladder is a sharply-circumscribed, more or less circular defect in the mucous membrane, with a dirty-yellow, "bacony" infiltration of its base and edges. On closer examination, this bacony infiltration proves to consist of "true" tubercles; miliary nodules, some grey, some cheesy, packed closely together, form the floor and edges of the ulcer, while the youngest and smallest granulations serve to extend the process, and are scattered, far in advance of the rest, through the healthy parenchyma of the mucous membrane. In fact, the growth of miliary tubercles takes the place of the "plastic infiltration" of common inflammation; while their cheesy metamorphosis, softening, and disintegration, stand for the subsequent destructive suppuration. Side by side with the older and mature ulcers, we usually find the first beginnings of the disorder in the form of solitary, grey or cheesy, miliary nodules, disseminated through the most superficial layer of the connective tissue of the mucosa; others again, forming small clusters, and already exhibiting a minute central cavity. The gradual and uniform extension of the growing and softening tubercles from these centres, necessarily gives rise in the first place to a circular ulcer, the "lenticular tuberculous ulcer." Several such ulcers, becoming confluent, form secondary ulcerations of larger size, whose outlines are most irregular. These gradually extend over progressively wider areas of the mucous surface, until at length the denuded parts exceed the healthy surface in amount, the relatively intact portions forming narrow borders between adjoining ulcers.

§ 385. These observations, which primarily refer to tuberculosis of the urinary bladder, may be transferred to any part of the uro-genital tract, and particularly to the lining membrane of the ureters. The anatomical appearances in the latter case however, are markedly complicated by the introduction of a catarrhal element. The tuberculous ureter is at first only in a state of catarrh; the swollen mucous membrane pours out a thick, viscid, purulent secretion; and the swelling, together with the discharge, may affect the state of the urine, causing the chief clinical symptoms of tuberculous disease of the ureters, before a single tubercle is formed. Tuberculosis of the womb is secondarily complicated with an overgrowth of the connective tissue, partly in the submucous, partly in the muscular layer, which may attain very considerable proportions; hence a positive enlargement of the organ as a whole, is associated with a progressive loss of substance from its inner surface. Even more peculiar is the complication of tuberculous ulceration of the bowels with a papillary and polypoid hypertrophy of the unaffected residue of the mucous membrane. This may assume such proportions, that the entire membrane may be masked by the dark-red, congested polypi, as large as peas, between whose bases the ulcerated surface itself may escape notice unless looked for. The complication is not, however, a common one. Far more common, and much more difficult to distinguish from the tubercular affection proper, is the combination of tuberculosis with that scrofulous overgrowth of the lymphatic follicles with which we have already become familiar, as it occurs in the lymphatic glands (§ 203, *et seqq.*).

§ 386. The very same regions of the digestive system which we found to be affected in abdominal typhus, are also the favourite seat of tuberculosis, *sc.* the lymphatic glands, Peyer's patches, and solitary follicles in the neighbourhood of the ileo-cœcal valve. The process however is not restricted, as in abdominal typhus, to the lymphatic structures and the parts immediately surrounding them; it starts from them indeed, but only to extend farther according to a special law of its own. Now it is just these primary changes in the closed follicles which are not of a tuberculous nature. The grey intumescence which causes enlargement of the individual follicle to about three times its normal bulk, depends upon the same one-sided kind of proliferation of the corpuscular elements in the lymph-paths and the reticular parenchyma of the follicles, with which we are familiar as the cause of the scrofulous bubo; the subsequent caseation, it is true, differs in no respect from the degenerative change to which the true tubercles themselves succumb; so that when once this stage has been reached, it is no longer possible to distinguish between the two processes. It is worthy of note, moreover, that the disorder of the corresponding mesenteric glands is purely of a "scrofulous" kind, and cannot be confounded with the very different anatomical appearances presented by genuine tuberculosis of a lymphatic gland.

The cheesy follicles soften from without inwards, and when the cheesy matter is wholly dissolved, we find a sharply-circumscribed hemispherical defect, the so-called "cleansed ulcer," environed by relatively healthy tissue. The close proximity of the neighbouring follicles to one another in a Peyer's patch, may lead, even at this early stage, to a coalescence of several of these minute ulcers to form those larger defects which, from their being bounded on all sides by segments of a circle, with their convexities outwards, have been called "racemose ulcerations."

§ 387. On examining fine vertical sections through the base and edges of one of these ulcers, we notice that it is everywhere surrounded by a tolerably wide zone of corpuscular infiltration of the connective tissue. But neither in the corpuscular elements themselves, nor in the mode of their arrangement, can we detect anything specific. It would seem, moreover, that the gradual extension of the ulcer is essentially due to the progressive advance of the infiltration into the neighbouring tissues, and the subsequent resolution of the infiltrated matters upon the ulcerated surface. The specific, "tuberculous" element, is accordingly quite subordinate in tuberculosis of the intestines. But it would be a great mistake to suppose it wholly absent. Careful investigation shows—1st, The presence of a certain number of miliary nodules in the tunica adventitia of all the non-capillary vessels, and especially of the arteries in the neighbourhood of the ulcer. 2nd, The strictly tuberculous nature of those granulations which occasionally spring up on the opposite surface of the intestinal wall, in the subserous and serous connective tissue, and which enable us to ascertain from the outside, the exact position of the morbid changes in the mucous membrane. The observations recorded in § 115, led me to investigate these structures very thoroughly; and I have assured myself that here too, it is the lymphatics which undergo tuberculous degeneration, and that the sheaths of the vessels are so manifestly chosen by the tuberculous products, only because they also contain the efferent lymphatics of the bowel.

The development of miliary nodules upon the branches of the vessels or lymphatics is of especial moment in the present instance, inasmuch as it determines the direction in which the ulcer of the intestinal mucous membrane must extend. For, in marked contrast to the invariably axial configuration of the typhoid ulcers, which do not overstep the limits of a Peyer's patch, the tuberculous ulcers exhibit a decided tendency to spread transversely. They are always tending to become zonular; originating in Peyer's patches, where also they attain their greatest width, they push their way over the lateral margins of the patch, till their extremes unite on the opposite side of the bowel. If we compare the distribution of the blood-vessels with this mode of extension, we cannot fail to see a certain parallelism between them. The arteries and veins reach the bowel between the layers of the mesentery, on the side opposite to the Peyer's patch; from this point they radiate in an arborescent form, their trunks and main branches coursing transversely across the intestinal tube, while their finer ramifications meet on the outer side of the canal, where the patches are situated. The vascular territories of the intestinal wall are accordingly transverse and not axial, and any morbid change which is conterminous with a vascular area, must *eo ipso* extend in a transverse direction.

Now the discovery of miliary nodules upon all the ramifications of the afferent vessels makes it clear that tuberculosis belongs to this category; hence too, we see why it extends across, and not along the bowel.

§ 388. As regards the further consequences of tuberculous ulceration of the bowels, I need only say that hæmorrhage and perforation may occur, just as in abdominal typhus. The tuberculous infiltration of the vascular wall on the one hand, and of the serous membrane on the other, and the necrobiotic detachment of the infiltrated part, necessarily lead to perforation, now into the blood-channel, now into the peritoneal sac. In either case however, this accident presupposes the absence of those natural safeguards which usually ward off any such extreme issues; in the former instance, timely coagulation of the blood in the endangered vessel, in the latter, timely adhesion of the serous coat to some other part of the peritoneal surface. I have seen a case in which five tuberculous ulcers of the ileum had perforated, not however into the peritoneal sac, but into other divisions of the bowel, which had previously become adherent opposite the seat of ulceration. This, of course, put a stop to all peristalsis, the products of digestion circulating without any order through numerous false passages in the abdominal cavity, inasmuch as the fistulous communications were in some cases wider than the calibre of the intestinal tube itself.

§ 389. Passing now to tuberculosis of the LARYNGEAL and BRONCHIAL mucous membranes, we enter on a debateable ground, where it becomes extremely difficult to ascertain how much of the morbid process is really tuberculous. *Virchow* does not scruple to assert that "tuberculous" ulcers of the larynx actually originate from miliary tubercles; he assigns their production, and extension both in breadth and depth, to a process identical with that which we learnt to know in connexion with tuberculous ulceration of the mucous lining of the urogenital tract. Other observers, as *e.g. Rühle*, utterly deny the presence or participation of miliary granulations in the process; indeed *Virchow* is at the pains to explain, that miliary nodules are so rarely to be detected in these "tuberculous" ulcers, only because they are here especially frail and perishable: this explanation is equivalent to an admission that they are very seldom to be seen.

Now if we undertake a painstaking histological analysis, by examining vertical sections through the affected parts of the laryngeal and tracheal mucous membranes, and endeavour to eliminate whatever is decidedly non-tuberculous, we must begin by refusing a specific character to any morbid change in the closed follicles. The larynx proper, indeed, is not, strictly speaking, furnished with closed follicles; but they are plentiful above the epiglottis, at the base of the tongue, on the isthmus faucium and the upper part of the pharynx; and tuberculous ulceration of the larynx proper is very commonly associated with ulcers due to scrofulous inflammation, proliferation and disintegration of these pharyngeal follicles. Further, the laryngeal and tracheal ulcerations which start from the orifices of the mucous glands, are not to be considered tuberculous. I have elsewhere explained more fully (§ 356) how chronic catarrh of the mucous membrane may give rise to dilatation and hypertrophy of the mucous glands. I will now proceed to describe another way in which these organs may become involved in chronic catarrhal alterations of mucous surfaces; and this is one which, hitherto at all events, I have only met with in this particular region and in this particular case. Accordingly I must regard it provisionally, as peculiar to the laryngo-tracheal mucous membrane, and more especially as a very important factor in that aggregate of anatomical changes which we include under the name of laryngeal phthisis.

If we separate the cut edges of a trachea whose mucous lining is in a state of chronic catarrhal inflammation, and wipe away the mucus from its surface, we may readily detect with the naked eye, the orifices of the mucous glands. In the intervals between the cartilages they are very closely set; here too, they are especially wide; on a level with the rings they are fewer in number and more narrow; here and there, indeed, they may even be quite absent. Now if we squeeze the trachea gently from below, these openings are seen to exude small quantities of viscid mucus, which present a sharp outline and resemble grey, translucent dewdrops. Should any one of these drops, on more careful inspection, exhibit a narrow straw-coloured border, this indicates that the ulceration in question has already begun. For this yellowish border consists of pus, pus produced by the subepithelial connective tissue of the follicular duct, and discharged into its cavity. During the extrusion of the accumulated secretion from the gland, this little drop of pus was the first to escape; it then became uniformly spread out round the edges of the drop of mucus which followed it. The pus-formation in the efferent duct may continue for a time as a purulent catarrh, but it must certainly pass, and that soon, into a pus-formation with loss of substance—into ulceration. A circular, shallow, funnel-shaped ulcer is formed, girdled by a narrow zone of a bright-yellow colour, which marks it off sharply from the hyperæmic mucous membrane round it. In the centre of this defect, the dilated orifice of the duct, or the gland itself after suppurative destruction of its elements, forms a rounded hollow of proportionate size, which is, at the same time, the deepest part of the floor of the ulcer; thus we see that the catarrhal ulceration of the gland-ducts is really peculiar enough to warrant our distinguishing it from allied conditions. It is only when the ulcer proceeds to extend in depth and breadth that its primordial characters become effaced. The coalescence of contiguous ulcers produces *e.g.* racemose outlines, like those which are usually held to be characteristic of the "tuberculous" ulcer; indeed the racemose form is even more distinctly marked in these cases than in tuberculous lesions of the bowels. The extension of the ulcer in depth, is favoured by the suppurative destruction of the body of the mucous gland. A suppurative inflammation of its capsular and interstitial connective tissue, leads to the disintegration and solution of the acini; the entire gland melts away; and when we reflect that the mucous glands of the air-passages are situated, not in the mucous, but in the submucous layer, we can readily perceive that these ulcers must be especially prone to produce "excavations." As a fact, we soon find the floor of the ulcer close to the tracheal rings, or the laryngeal cartilages; and this paves the way for a fresh series of lesions.

The cartilages of the larynx and trachea, owing to their non-vascular texture, and their obviously sluggish nutrition, are more disposed to undergo necrosis *en masse* than a gradual destruction by successive layers. When the inflammatory irritation reaches the perichondrium, it not unfrequently happens that before the cartilage itself has time to undergo any marked alteration in its form, colour and consistency, the entire mass is isolated by a suppurative perichondritis; it becomes a sequestrum, and is ready for expulsion, as soon as the abscess-cavity communicates with the floor of the ulcer by an aperture large enough to allow of its passage. (Arytænoid cartilages.) As a general rule indeed, this catastrophe is preceded by a stage of true ulceration; the cartilage is laid bare, though only on one side, that which forms the floor of the ulcer—while everywhere else the perichondrium continues intimately united to its surface. The advance of the destructive process may then be admirably traced in vertical sections; the outermost layers of cartilage-cells are transformed by fission into groups of pus-cells, while the cartilage-cavities have simultaneously increased in size at the expense of the matrix to such a degree, that just before they burst they are actually in contact with one another. Hence the floor of the ulcer, so far as it lies in the cartilage, is lined throughout with dilated cartilage-capsules full of pus. Meanwhile these alterations, though very important, are confined within relatively narrow limits. The third or fourth row of cartilage-cells (counting from the floor of the ulcer) is quite intact; at most, the nuclei may be beginning to divide. In the trachea, the course of the ulceration may lead to the denudation of the majority of the rings on their inner surface; one ring after another becomes detached from its extremities to its centre; the separation extending inwards till it is complete, when the entire ring is coughed up.

§ 390. Seeing that the most severe and extreme lesions of the larynx and trachea may be produced by simple catarrhal inflammation and ulceration, we may be tempted to inquire what there is left for tuberculosis to accomplish? Are tubercles present at all in "laryngeal phthisis"? and if present, what part do they play? It is quite clear that my own observations are opposed to any unconditional transfer of the results, arrived at by studying tuberculosis of the urogenital mucous membrane, concerning the mode of origin and extension of "tuberculous" ulcers, to the mucous lining of the larynx. On the contrary, I feel bound to insist that the actual destruction in the latter case is operated, not by the breaking-down of tubercular deposits, but by the known resources of inflammatory proliferation. Nevertheless, I am quite convinced, that here too, miliary tubercles may undoubtedly be developed; grounding my belief partly on the authority of *Virchow*, who has actually observed true "tuberculous" ulcers in the larynx, partly on certain appearances seen in vertical sections through the ulcers described above, appearances which I may be allowed provisionally to regard as due to an eruption of miliary granulations. For in these ulcers of the larynx and epiglottis, we very frequently meet with spheroidal clusters of cells, situated well below the surface, in the midst of connective tissue which is still intact. These deposits resemble a single gland-acinus in size; when soaked in carmine solution, they absorb the colouring-matter far more greedily at their edges than towards their centre, a fact which points to a globular mode of grouping, and reminds us very forcibly of the behaviour of miliary tubercles under the same conditions. These tubercles, indeed, are so sparingly disseminated, they appear so very insignificant in comparison with the inflammatory infiltration of the ulcerated surface itself, that I would only regard them as a pledge of the connexion of the morbid changes with constitutional tuberculosis. At most, they could only be raised to the dignity of permanent inflammatory irritants, and so made responsible for the obstinacy and proneness to recur which is so especially marked in these catarrhal inflammations.

The occurrence of true miliary tubercles on the minute bronchi, in the neighbourhood of so-called tuberculous cavities, will be discussed in the chapter devoted to the respiratory organs.

d. TUMOURS.

1. *Papillomata.*

§ 391. Papillomata of the mucous membrane must be carefully distinguished from those tuberous and polypoid elevations of the mucous surface, which are due to glandular hypertrophy and dilatation. They exhibit many varieties of external form and situation.

a. On the mucous lining of the oral cavity, in the vagina, just within the anus, in a word, on the transitional semimucous surfaces, we find the papillary types of the skin but little modified. Instead of the ordinary wart we have roundish, sessile, berry-like bodies, attached to the gums or the inner surface of the cheeks; they are very similar to condylomata, differing only in the greater toughness of their epithelial covering. Condylomata, both flat and pointed, occur in forms whose purity of type is proportional to the resemblance of the autochthonous epithelium of the affected part, to that which clothes these tumours. Nevertheless, the pointed condylomata keep very strictly to the muco-cutaneous boundary-line; while the broad and flat variety is met with here and there, both in the oral cavity and in the vagina.

b. On the mucous membrane of the gall-bladder, the urinary bladder, and the os uteri externum—in regions, therefore, which are normally lined with columnar or transitional forms of epithelium—the papillomata are also invested with columnar epithelium.

Papilloma of the bladder, also called villous cancer, or more correctly, villous tumour of the bladder, always springs from the trigone between the openings of the ureters. At this point a rounded, very soft tumour rises from a broad base to a height of about an inch above the mucous surface. It is clothed with so thick a layer of columnar cells, that the very wide capillaries which shine through, only succeed in giving it a rosy tint, making the entire mass look not unlike an encephaloid tumour (Markschwamm). In point of fact, however, the growth has nothing whatever to do with cancer; on the contrary, the most superficial examination is enough to show that it consists of a number of arborescent groups of villi, and of nothing else. This quite agrees with recorded cases of extirpation of papillomata of the urinary bladder, not followed by any return of the disease. Each of the component villi is characterised, on the one hand by containing an enormously wide and very thin-walled blood-vessel in its axis, which forms a loop with a varicose dilatation at its flexure, on the other by the triple or quadruple stratum of columnar cells already alluded to, which lie so close upon the vessel that the villus cannot justly be said to possess a framework of connective tissue at all.

Papillomata growing from the external os, contain more connective tissue and fewer blood-vessels; their epithelium too is more scanty. The stout, club-shaped terminations of the dendritic growth, are clothed with a single layer of columnar cells; nothing like a varicose dilatation of the vessels can be anywhere discerned. The description of "papilloma cysticum" given in § 70 is taken from this variety.

In the human gall-bladder we only meet with excessively minute and insignificant papillomata. On the other hand, *Virchow* has placed upon record the case of a cow, whose gall-bladder he examined; its thickened walls "were beset with such multitudes of partly villous, partly cylindrical, solid outgrowths, that the mucous surface over a certain area seemed to have entirely disappeared."

§ 392. The relations of these papillomata to epithelial cancer of the mucous membrane, are both interesting and important. Not only has it been shown that a papilloma may pass into an epithelioma, and that an epithelioma may be secondarily complicated by papillary proliferation from the edges and base of the ulcer, but it has been repeatedly asserted that the mucous membrane over a cancer which is forming in the submucous tissue, is prone to become the seat of papillary growth. For my own part, I have never observed anything of the kind, and I cannot therefore express any opinion concerning the intimate connexion of these two phenomena. *Virchow* regards the development of the papillomata as a simply hyperplastic change to begin with, excited by the irritation of the adjoining cancerous formation; the possibility of its conversion into a true VILLOUS CANCER only beginning, when the carcinoma is propagated by continuous infiltration from below, to the connective tissue of the papillæ. He goes on to say, that the stomach and urinary bladder are the chief seats of these true villous cancers, which are probably identical with our own columnar epitheliomata.

2. *Carcinomata.*

§ 393. The mucous surfaces, lined as they are with epithelium, are everywhere disposed to the production of epitheliomata; to that of glandular cancer only in so far as they happen to contain open glands. To this latter circumstance must be ascribed the striking differences between the average liability of various regions of the mucous tract to cancer. Moreover, the epithelial form seems to prefer the points of junction between the several divisions of the mucous tract; this is mainly owing to the pre-eminent exposure of such localities to mechanical irritation of some sort, which need not necessarily be abnormal.

§ 394. Starting from those orifices of the mucous system which are situated in the head, we find, apart from those cancerous affections of the lips, eyelids, and alæ nasi, which properly belong to the skin, a true soft glandular cancer of the MUCOUS LINING OF THE NASAL FOSSÆ. In adults, this is developed on a soil previously made ready for it by a chronic hypertrophy of all the structural elements of the mucous membrane; in children, it occurs without any preparatory stage. It forces its way by preference into the antrum of Highmore, distends the upper jaw, and manifests itself as one of the several varieties of what is known as "cancer of the upper jaw." The patient succumbs so rapidly to the attendant cachexia, that surgeons are now very shy of all operative interference. The tumour is wholly made up of imperfectly developed gland-tubuli, produced by an excessive proliferation of the epithelium of the mucous follicles.

§ 395. In the ORAL CAVITY, the tongue is a favourite seat of cancerous disease. It usually takes the form of a squamous epithelioma, which however, in accordance with the greater delicacy of the normal squamous epithelium of the tongue, is distinguished from the harder squamous epitheliomata of the skin by its softness, and a tendency to speedy disintegration. The quantity of blood-vessels, lax areolar tissue, and above all, of wide lymph-paths with which the tongue is furnished, renders its parenchyma peculiarly favourable to an extension of the morbid growth by infiltration. Hence the local mischief assumes a foremost place in the history of the disease. The primary nodule is nearly always situated on one or other edge of the tongue. It is said that the irritation of a ragged and decaying tooth may have some share in causing the cancer. This primary nodule is usually extirpated by a V-shaped incision. The disease soon recurs however, and the operation has to be repeated; with each repetition, the interval between the extirpation and the return of the disease grows shorter, until at last the entire tongue is destroyed. Metastatic deposits may occur both in the nearest lymphatic glands, and in the lungs; these secondary deposits however, are always of very subordinate importance.

What is known as soft cancer of the tonsils, is a soft lymphadenoid sarcoma which is very prone to invade the palatine arches and the isthmus faucium (Choanen).

§ 396. At the entrance to the RESPIRATORY TRACT we meet with a tolerably soft variety of squamous epithelioma, which differs from that of the tongue in its tendency to develope papillary outgrowths. In the substratum of the laryngeal mucous membrane, the tumour meets with a soil as ill-adapted as possible for any extension by way of infiltration. Next to a submucous layer made up of perfectly inelastic fibres, comes one of fibroid tissue; beneath this, and throughout the whole of the submucous and mucous layers, networks of elastic fibres are abundantly distributed. What wonder then if the growth tend rather to extend outwards, to form papillary excrescences, for years and years before it penetrates into the deeper structures of the neck?

§ 397. In the ŒSOPHAGUS, a hard squamous epithelioma gives rise, first to a zonular tumour, and then to a zonular ulcer with an infiltrated base and edges; the ulcer extends; the mucous membrane may come to be deficient all round the tube for a width of two to three inches; while the base of the ulcer may invade, and eat its way into, the neighbouring air-passages from without. A perforation through the floor of the ulcer into the respiratory passages is a very grave accident. This abnormal communication between the alimentary canal and the respiratory passages is usually situated, not in the trachea, but in the posterior wall of the left bronchus. The left bronchus, as is well known, crosses the œsophagus in its middle third, and this is the point usually selected by œsophageal cancer. It has justly been supposed that a mechanical cause of some kind must contribute to localise the disease at this particular point; and that cause is to be sought in the fact that every morsel of considerable size, in passing down the œsophagus, squeezes its anterior wall against the posterior wall of the unyielding bronchus. Of course perforation of the air-passages is only one among many dangers to which the victim of œsophageal cancer is exposed. The zonular tumour may prove fatal by causing stricture; the extension of the morbid process to the mediastinum may, during the inspiratory fall of tension in the thoracic cavity, occasion the entrance of air from the œsophagus into the lax areolar tissue which adjoins it, and so give rise to true emphysema of the entire subcutaneous tissue; the base of the ulcer may become converted into a regular diverticulum, in which the food may lodge and become decomposed, &c.

Compared with carcinoma of the middle third of the œsophagus, cancerous affections of the cardia and other regions are uncommon. I have met, however, on two separate occasions, with a very superficial and much softer variety of cancer, which had invaded large sections of the œsophageal tube in a very diffuse way.

§ 398. The STOMACH has an especially rich *répertoire* of carcinomata; we find, with nearly equal frequency, a soft, a hard, and a colloid form of glandular cancer, as well as a columnar epithelioma. All the varieties of glandular cancer agree in their origin from the mucous membrane proper, extending secondarily to the submucous tissue. I lay stress upon this fact, because an essential distinction used to be drawn between "submucous" and "mucous" cancers of the stomach. It is true that the transition above alluded to usually occurs at a very early period, and that the cancerous proliferation advances much more rapidly in the wide spaces of the submucous tissue, with their numerous lymphatic networks, than in the mucosa proper. Hence it is, therefore, that the cancer frequently takes the form of a laminar infiltration of the wall of the stomach, over which the mucous membrane extends, either unaltered or simply atrophied, and is freely moveable, while it is bound down to the subjacent growth at one point only. Now it is from this point that the morbid process originally sets out; this is the oldest part of the disease. In most of the cases which come under our notice, it is occupied by an ulcer, which has destroyed the place of origin of the cancer, and has accordingly made it impossible to decide, whether the glandular elements of the mucous membrane had any share in the first development of the disease, or not. All the more valuable are the statements made by *Waldeyer* (*Virchow's* Archiv, vol. xli.), who succeeded, notwithstanding these obstacles, in establishing the origin of the morbid growth from the mucous follicles and peptic glands.

A very usual post-mortem appearance in *soft cancer* of the stomach, is that of a single ulcerated patch, several square inches in area, surrounded by a border of mucous membrane thickened by infiltration with cancerous elements. The tumour has originated, as very often happens, on the lesser curvature, and has extended downwards from this point both along the anterior and the posterior wall of the organ. The ulcerated surface itself is covered with shreds of tissue, which float when a stream of water is poured over them. They are the remains of the cancer-stroma, which resist destruction longer than the cancer-cells. They now become detached, principally owing to the action of the gastric juice, and so give rise to those pathognomonic hæmorrhages in which the blood escapes a drop at a time, coagulates forthwith, and assumes a brownish-black tint; innumerable particles of this altered blood giving the contents of the stomach — the vomited matters — the appearance usually described as resembling coffee-grounds, chocolate, &c. On examining a vertical section through the thickened border of the ulcer, we see how, on the sound side, the glandular layer of the mucous membrane is stretched by the tumour, how over the most prominent part of the raised border its thickness is suddenly reduced, the glands being as it were compressed at both ends, and the contiguous ones forced asunder. At last the mucosa proper is only represented by an interrupted chain of wasted glands; between which and the muscular coat, the entire thickness of the cancerous mass, which may attain from four to six lines, intervenes. On the other side of the boundary, the transition to ulceration is effected by fatty degeneration of the cancer-cells. Even the unarmed eye can detect the yellow dots and striæ of the decaying cancer-tissue, and trace them all round the floor and borders of the ulcer. The disintegration itself may be hastened by the action of the gastric juice upon the necrobiotic tissue; at least the process is usually more sluggish in the precisely analogous affections of the uterus, urinary bladder, &c.

The course of *scirrhus ventriculi* is very different. This variety of cancer is far slower in its rate of growth; starting from the lesser curvature, its favourite place of origin, it succeeds for the most part in extending round the entire circumference of the stomach. The submucous and mucous layers are converted into a white, fibroid band, from two to three lines thick, which, when the girdle is complete, gives the middle of the stomach the appearance of a rigid tube from one to two inches in diameter, to which the fundus is attached like a loose bag. The microscope shows a very marked resemblance between the arrangement of the epithelial elements and that of glandular epithelium. Not that the cells and cell-nests are either very large or very numerous; on the contrary, the stroma of connective tissue decidedly predominates. But the form of the cell-nests is comparatively regular; they are elongated tubuli, circular in transverse section, in which the epithelial elements, of small but uniform size, are disposed almost radially, though an axial lumen may not be discoverable.

Colloid cancer of the stomach is also distinguished by its prevailing tendency to cause destruction, as opposed to ulceration; even before giving way, it invariably becomes zonular. It may thus give rise to very serious stenosis. The ulcerative process is a slow disintegration, proceeding from within outwards, without hæmorrhage or abundant secretion of any sort. Were it not for the risk of extension to the peritoneum, colloid cancer of the stomach would agree with scirrhus in the comparative innocence of its primary manifestations.

As regards the minute structure of this form of cancer, the horizontal sections recommended by *Köster* are so far important, that they undoubtedly shift the onus of infiltrative propagation to the lymph-paths of the gastric walls. This observer is inclined to transfer the results which he has obtained from the investigation of Cylindromata (§ 173), with reference to the share taken by the endothelia in the process of morbid growth, to colloid cancer of the stomach. My notions concerning hard glandular cancer, as laid down in § 159, make it quite obvious, that I can have no *a priori* objections to this view. I would regard these appearances as indicative of an "epithelial infection" of the endothelial elements of the lymphatics, starting originally from the glands. But I must beg the reader to observe that my attitude, especially as regards the colloid variety of cancer, is one of expectation.

§ 399. THE SPREAD OF THESE THREE VARIETIES OF CANCER OF THE STOMACH TO NEIGHBOURING ORGANS is of high clinical importance and anatomical interest. The muscular coat is involved after the submucous layer. The cancerous infiltration follows the narrow bands of interstitial connective tissue between the muscular fasciculi. These fasciculi themselves, owing perhaps to the continued irritation to which they are exposed, undergo a hyperplastic thickening. This is the rule at least in the colloid and scirrhous forms of cancer. In vertical sections through the walls of the stomach, we can trace, even with the naked eye, the progressively increasing thickness of the muscular bundles as we pass from the healthy to the diseased tissues. If we add to this the amount of additional matter produced by the cancerous degeneration of the interstitial tissue, we can be at no loss to account for the muscular coat attaining from three to five times its normal thickness.

Having traversed the muscular coat, the cancer reaches the visceral peritoneum. The first nodules then make their appearance in the subserous connective tissue. Their arrangement often shows very clearly their original dependence on the course of the muscular fasciculi; *i.e.* they lie parallel to these, in lines which correspond to the intermuscular septa of connective tissue. Soon, however, the adjacent nodules coalesce with one another, and we get irregular, flattened lumps, which present the special characters of the particular variety of cancer to which they belong, in their least complicated form.

This extension to the peritoneal coat is almost always the signal for a general degeneration of the entire sac. It is probable that the mutual friction of the viscera may detach bits of the cancerous nodules and carry them hither and thither over the smooth surfaces of the membrane, until they find their way into some fold or recess where they give rise to the development of a fresh nodule. The general effect—as *Virchow* puts it—is that of seeds having been scattered over the peritoneal surface, falling here and there, and germinating. In this respect, soft and scirrhous cancer behave in precisely the same way. The colloid variety takes up a position of its own in this as in other matters; it performs the giant task of converting the whole peritoneum into a mass of colloid cancer, continuously, without any break, by a simple process of infiltration. The thickness which a single peritoneal lamina attains when the infiltration is completed, amounts to two or even three lines; the omentum, as a duplicature of the membrane, is converted into a plate an inch thick, and as hard as a board; the mesentery and the various ligaments follow suit. It is self-evident that under such conditions, the most important disturbances of peristaltic action are unavoidable. The phenomena are usually complicated, moreover, by inflammatory accidents, by an abundant sero-fibrinous exudation, by small hæmorrhages and adhesions. Similar accidents also occur in the course of soft and scirrhous cancer. The scirrhous variety however, exhibits a very remarkable peculiarity in addition, doubtless connected with minuter tissue-changes, but the main feature of which has hitherto evaded all direct elucidation. I refer to the contraction of the connective tissue in the neighbourhood of the scirrhous nodules. The narrowing of the gastric cavity, which coincides in point of time with the thickening of its walls, and which has already been alluded to, must be ascribed to this contraction. In this locality however, there is no hope of ever arriving at a better knowledge of the process. The phenomena are far more open to investigation as they occur in the peritoneum. We may expect, in particular, to get at some reliable results by examining the transparent texture of the epiploon. This, in point of fact, shrinks into a rigid cord, with cancerous nodules scattered through its substance, which may even, supposing the ascites moderate in amount, be felt through the abdominal walls in the region of the transverse colon. If we spread it out, and try to ascertain the cause of its shrinking, it reminds us, under a low magnifying power, of a cloth, spread out flat, and then clutched and crumpled together from a single point, from which the folds all radiate; but instead of the crumpled nucleus, we find the smooth, white, scirrhous nodule, forming the centre of these radiating folds. For my own part, I feel convinced that the pre-existing connective tissue really is in some sort used up in the present case, and that the scirrhous nodule, moreover, represents the quantity of connective tissue so employed; but I am not able to offer any opinion about the way in which this is brought to pass.

This degeneration of the peritoneal sac naturally leads to rigidity and contraction of the mesentery, and consequently to the most serious disturbances of the intestinal peristalsis; moreover, very intimate adhesions usually form between the abdominal viscera, so that the small intestine, for instance, is often found as it were rolled up into a ball, in the interior of which its canal forms the most labyrinthine convolutions, offering difficulties, almost insurmountable to its being traced out by dissection.

§ 400. Instead of the various forms of squamous epithelioma which we have repeatedly encountered between the lips and the cardiac orifice, we meet, below the cardia, with a *columnar epithelioma.* Its favourite seat is in the stomach, and most commonly in its pyloric part; indeed it is often localised on the fold of mucous membrane which separates the stomach from the duodenum. In this region it gives rise in succession, to a flat tuberous elevation, a fungoid tumour with a broad base, and finally a polypus; the latter is often quite spherical, larger than a pigeon's egg, with a relatively short pedicle. In this its final form, the tumour is admirably fitted to block up the duodenal canal, and so, *i.e.* by hindering the introduction and digestion of food, to cause acute marasmus ending in death, unless the growth is speedily softened and broken up. When this occurs, a smooth excavation is left, in whose edges the further extension of the growth may be traced. And here it is closely related to that adenoma of the alimentary tract which I have described more fully in § 171.

§ 401. In the lower divisions of the digestive tube, we have a soft glandular cancer of the COLON, which tends to produce zonular ulcerations with a fibroid and therefore firmly-contracted base, and so to cause stricture of the bowel with its consequences. In the same region we find a superficial adenoma—a variety which is also met with in the rectum (*Klebs*, *Leyden*). Squamous epitheliomata of the RECTUM immediately above the anus, frequently attain a very considerable size as cauliflower growths, before they start from the mucous follicles to invade the deeper parts (cf. § 166, *note* 2).

§ 402. The UTERUS exhibits a greater liability to cancerous disease than any other part of the urogenital tract (if we class cancroid of the penis among tumours of the skin). A good half of all the cases of so-called uterine cancer are epitheliomata. These originate either from the mucous lining of the cervix or from the portio vaginalis; in either case, it is long before the boundary-line between the portio vaginalis and the canal of the cervix is overstepped. Cancroid of the portio vaginalis very commonly originates as a soft papilloma, or cauliflower growth; the transition to deeper parts being effected, as in papillomata of the skin, by the dislocation of the epithelial boundary into the subepithelial connective tissue. Epithelial cancer may give rise to very extensive lesions in the uterus. The muscular coat offers most resistance. When this has given way, the lax areolar tissue between the organs of the true pelvis offers a most favourable soil for the luxuriant extension of the morbid growth. We find a cavity several inches in diameter, whose internal surface is coated with the most offensive products of putrefaction, bounded above by the still undestroyed remnant of the fundus uteri, in front by the posterior wall of the bladder, behind by the anterior wall of the rectum; while the vagina, whose upper half is also involved in the destructive process, maintains the cavity in communication with the exterior. At a later period, perforations occur in the floor of the ulcer; that which lays open the bladder gives rise to a vesico-vaginal fistula, that into the rectum, to a recto-vaginal fistula, while the perforation of the peritoneal sac excites peritonitis. It is this latter accident indeed, which often brings the lamentable sufferings of such patients to a close.

§ 403. The glandular cancers of the womb are situated in the body of the organ. They cause its enlargement, which is often considerable and tolerably uniform; the true pelvis is filled up, the rectum and bladder compressed and displaced. On opening the organ, its cavity is found to be distorted by the cushion-like convexity of its protruding walls; the walls themselves, throughout their entire thickness (up to 3 inches), are of a uniform marrowy-white colour; the line of demarcation between the mucous and muscular coats is obliterated, the proliferating gland-tubuli having made their way through the entire thickness of the latter layer.

§ 404. In the URINARY BLADDER, the villous cancers which grow from the trigone are especially worthy of note (*see* § 392). Besides these, a squamous epithelioma is occasionally, though rarely, met with in the calyces and pelves of the kidneys. It usually extends at a comparatively early period to the tips of the adjoining papillæ, and spreads, forming a milk-white zone of infiltration from two to three lines in thickness, into the renal parenchyma—a true "phthisis renum cancrosa."

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